

Report on Dill

11/17/72

DILL

REPORT

ACCESSION NO. 19

DILL


CAS REG. NO. 977050604

GRAS Review Branch (BF-335)
Bureau of Foods
Food and Drug Administration
200 C Street, S. W.
Washington, D. C. 20204

Submitted to Att: Mr. Alan Spiher,
Project Manager

Date November 17, 1972

Laboratory No. 1216


Howard Feinman, Director
Biological Sciences

Food and **D**rug **R**esearch **L**aboratories
INCORPORATED



Maurice Avenue at 58th Street
Maspeth, New York 11378

TABLE OF CONTENTS

<u>SUBJECT</u>	<u>PAGE</u>
Summary	1
Chemical Information	2
Bibliography	12
Reference Articles	Section II

DILL OIL

Summary

There is a decided paucity of information in the literature pertaining to the question of dill oil toxicity.

An NAS/NRC report (26) on spice toxicants includes dill in the list of condiments in which the safety factor between levels that are organoleptically acceptable and those that are harmful is small, or the toxic constituent is effective at low levels. The only toxicant mentioned is myristicin but perhaps the coumarin type compound found in dill extracts(4) should also be included. Coumarin is reported to cause liver damage(26a), and myristicin, which also damages the liver, is in addition a narcotic and psychomimetic agent.(54)

Dill Oil has been shown to have a spasmolytic action on the smooth musculature, antagonizing spastically active substances such as acetylcholine, histamine, serotonin, etc. In experiments with isolated strips of rabbit and guinea-pig intestine, isolated guinea-pig lungs, cat lungs "in situ", as well as guinea-pigs under condition of anaphylactic shock, it was concluded that the calming action of the oil is chiefly myotropic.(49) It has also been historically used as an aromatic carminative.(56) In hemorrhoidal cases, enemas containing a 10% solution of dill extract have been found to induce the rebuilding of damaged tissue.(19)

DILL

Chemical Information

I. Nomenclature

A. Common names (17a, 18a)

- . Dill
- . Dill Seed
- . Oil of Dill

- . Dill Seed Oil, Indian
- . Dill Seed Oil, East Indian
- . Dill Oil, Indian

- . Dillweed Oil, American; Oil Dillweed American
- . Dill Oil; Oil Dill
- . Dill Herb Oil; Oil Dill Herb

- . Dill Seed Oil, European

B. Chemical names

(none)

C. Trade names

(none)

D. Chemical Abstracts Unique Registry Numbers

Dill - 977050604 Dill Oil - MX8006755

Dillweed Oil, American - 977050626

Dillweed Oil, European - 977053001

Dill Seed Oil, Indian - 977050615

II. Empirical formulae

Dill oil is a mixture of substances with the major components being (38a):

Carvone: $C_{10}H_{14}O$

d-Limonene: $C_{10}H_{14}$

α -Phellandrene: $C_{10}H_{16}$

β -Phellandrene: $C_{10}H_{16}$

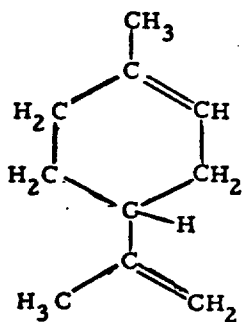
The Indian Dill Oil contains in addition (40a):

Dill Apiole: $C_{12}H_{14}O_4$

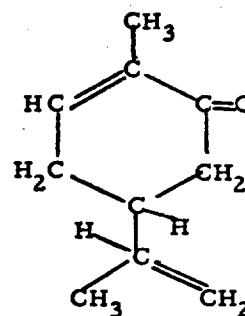
Dill-iso-Apiole: $C_{12}H_{14}O_4$

III. Structural Formulae

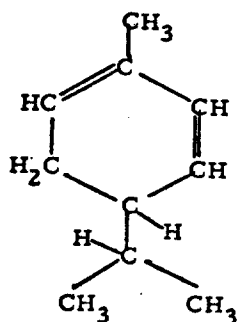
d-Limonene



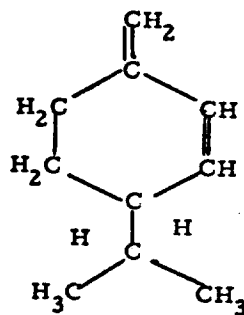
Carvone



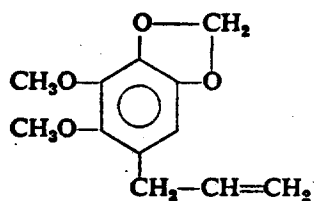
α -Phellandrene



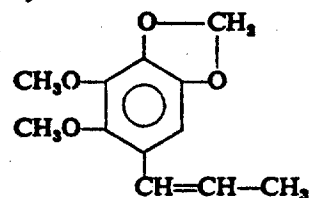
β -Phellandrene



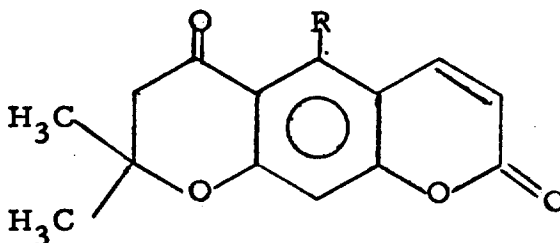
Apiole (1,2-Methylene dioxy-4-allyl-5,6-dimethoxybenzene)



iso-Apiole (1,2-Methylenedioxy-4-propenyl-5,6-dimethoxybenzene)



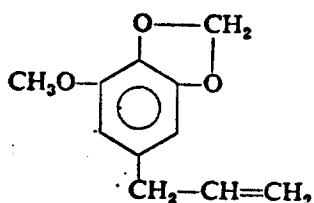
Recent work (4) describes the isolation of a new coumarin compound from the upper parts of the European dill plant. The structure is given as:



In addition the fruit of the Indian dill plant has been shown to contain quercitrin (approx. 500 ppm) and vitamin K. (20)

In dill herb oil, in addition to these substances, myristicin has also been identified as a component. (24a)

Myristicin



IV. Molecular weight-of identified components

Carvone - 150.11

d-Limonene - 134.11

α -Phellandrene - 136.13

β -Phellandrene - 136.13

Apiole - 222.24

iso-Apiole - 222.24

V. Specifications

A. Chemical

(none)

B. Food Grade (18a)

Dill Seed Oil, European:

Assay: Not less than 42 per cent and not more than
60 per cent, by volume, of ketones as carvone
($C_{10}H_{14}O$).

Angular rotation: Between $+70^\circ$ and $+82^\circ$.

Refractive index: Between 1.4830 and 1.4900 at 20° .

Solubility in alcohol: Passes test.

Specific gravity: Between 0.890 and 0.915.

Limits of Impurities:

Arsenic (as As). Not more than 3 ppm (0.0003 %).

Heavy metals (as Pb). Not more than 40 ppm
(0.004 %).

Lead. Not more than 10 ppm (0.001 %).

Dill Seed Oil, Indian:

Assay: Not less than 20 % and not more than 30 %, by
volume, of ketones as carvone ($C_{10}H_{14}O$).

Angular rotation: Between $+40^{\circ}$ and $+58^{\circ}$.

Refractive index: Between 1.4860 and 1.4950 at 20° .

Solubility in alcohol: Passes test.

Specific gravity: Between 0.925 and 0.980.

Limits of Impurities:

Arsenic (as As). Not more than 3 ppm (0.0003%)

Heavy metals(as Pb). Not more than 40 ppm(0.004%)

Lead. Not more than 10 ppm (0.001%)

Dillweed Oil, American:

Assay: Usually not less than 28% and not more than 45%
by volume, of ketones as carvone ($C_{10}H_{14}O$).

Note: Oil obtained from early season distillation
may show a carvone content as low as 25%
and a correspondingly lower specific gra-
vity, lower refractive index, and a higher
angular rotation.

Angular rotation: Between $+84^{\circ}$ and $+95^{\circ}$.

Refractive index: Between 1.4800 and 1.4850 at 20° .

Solubility in alcohol: Passes test.

Specific gravity: Between 0.884 and 0.900.

Limits of Impurities:

Arsenic (as As). Not more than 3 ppm(0.0003 %).

Heavy metals(as Pb). Not more than 40 ppm (0.004%).

Lead. Not more than 10 ppm (0.001%).

C. Official Compendia

Food Chem. Codex. 1st Ed. 1966.

VI. Description

A. General Characteristics (17a)

Dill Seed Oil, European: Slightly yellowish to light yellow liquid with a caraway - like odor and flavor. It is the volatile fraction obtained by steam distillation from the mature fruit or seeds. Its carvone content can vary from 42% to 60%.

Dill Seed Oil, Indian: Light yellow to light brown liquid with a rather harsh caraway-like odor and flavor. It is obtained by steam distillation of the seed and generally has a carvone content ranging from 20% to 30%.

Oil Dillweed, American: Light yellow to yellow liquid obtained by steam distillation of the freshly cut plant including stalks, leaves and seeds. Its carvone content ranges from 28% to 45%.

B. Physical Properties

Dill Seed Oil, European:

Specific Gravity at 25°/25° C: 0.890 to 0.915.

Optical Rotation: +70° to +82°.

Refractive Index at 20° C: 1.4830 to 1.4900.

Solubility:

Benzyl Benzoate: Soluble in all proportions.

Diethyl Phthalate: Soluble in all proportions.

Fixed Oils: Soluble in all proportions in most fixed oils.

Glycerine: Practically insoluble.

Mineral Oil: Soluble in all proportions.

Propylene Glycol: Soluble with slight opalescence.

Stability:

Acids: Relatively stable to weak acids.

Alkali: Relatively stable to weak alkali.

Oil Dill Seed, Indian:

Specific Gravity at 25° C/25° C: 0.925 to 0.980.

Optical Rotation: +40° to +58°.

Refractive Index at 20° C: 1.4860 to 1.4950.

Solubility:

Benzyl Benzoate: Soluble in all proportions.

Diethyl Phthalate: Soluble in all proportions.

Fixed Oils: Soluble in all proportions in most fixed oils.

Glycerine: Relatively insoluble.

Mineral Oil: Soluble in all proportions with occasional slight opalescence.

Propylene Glycol: Relatively soluble.

Stability:

Acids: Stable to weak organic acids.

Alkali: Relatively stable to weak alkali.

Oil Dillweed, American:

Specific Gravity at 25° C/25° C: 0.884 to 0.900.

Optical Rotation: +84° to +95°.

Refractive Index at 20° C: 1.4800 to 1.4850.

Solubility in Alcohol: Soluble in 1 volume and more
of 90% alcohol.

Stability:

Acids: Stable in the presence of weak organic
acids.

Alkali: Relatively stable to weak alkalis.

Solubility:

Benzyl Benzoate: Soluble in all proportions.

Fixed Oils: Soluble in all proportions in most
fixed oils.

Glycerine: Practically insoluble.

Mineral Oil: Soluble in all proportions.

Propylene Glycol: Usually soluble with opales-
cence or turbidity.

C. Stability in Containers :

Preferably in glass, tin-lined or aluminum containers.

Good quality galvanized containers are suitable when long
storage is not contemplated. Store preferably in tight, full
containers in a cool place protected from light.

VII. Analytical Methods

- . Identification and estimation of carvone and dillapiole by
GLC of a hexane extract (8).
- . Distinguish Indian dill (A. sowa) from European dill (A. gra-
veolens.) by TLC of petroleum extracts (10).

VIII. Occurrence and levels found in:

A. Plants

The oil represents the volatile fraction usually obtained by steam distillation either from the entire freshly cut plant, or from the crushed, dried fruit(or seeds). The European and American plant is identified as *Anethum graveolens*, the Indian as *A. sowa*. (18a)

B. Animals

(none)

C. Synthetics

(none)

D. Natural inorganic sources

(none)

DILL OIL

Biochemical Aspects and Biological Data

The pertinent biochemical and biological data found in the abstracts were deemed insufficient for inclusion into the usual monograph format.

DILL

Bibliography

- (1) Abdulov, A. G. and L. L. Lantsevitskaya. 1958. The vitamin-C content of Apsheron plants. Sbornik Trudov. Azerbaidzhan. Med. Inst. 4:218-221.
- (2) Alm, F. 1952. Effect of acetic acid on the oxidation of ascorbic acid in plant tissues. II. Various fruits and vegetables. Intern. Z. Vitaminforsch. 24:81-87.
- (3) Anderson, E. E. ; et al. 1953. Effect of essential oils on the inhibition and thermal resistance of microorganisms in acid food products. Fd. Res. 18:40-47.
- * (4) Aplin, R. T. and C. B. Page. 1967. Constituents of native Umbelliferae. I. Coumarins from dill (*Anethum graveolens*). J. Chem. Soc. 23: 2593-2596.
- (5) Arbusow, B. 1928. Untersuchung der Zusammensetzung des Terpentins von *Pinus silvestris*. I. J. Russ. phys. -chem. Ges. (russ.) 54: 267.
- (6) Baslas, R. K. ; et al. 1971. Chemical examination of essential oils from plants of genus *Anethum* (Umbelliferae) - oil of seeds of *Anethum graveolens*. I. Flavour Industry. 2(4):241-245.
- (7) Baslas, K. K. 1968. Chemistry of Indian essential oils. VII. Perfum. Essent. Oil Rec. 1968: 59(8):572-576.
- * (8) Betts, T. J. 1969. The carvone and dillapiole content of dill fruits by gas chromatography without preliminary distillation. J. Pharm. Pharmacol. 21(4):259-262.
- (9) Betts, T. J. 1965. Carvone in the developing fruits of *Anethum graveolens* and *Carum carvi*. J. Pharm. Pharmacol., Suppl. 17:41-43.
- * (10) Betts, T. J. 1964. Umbelliferous fruit identification by thin-layer chromatography. J. Pharm. Pharmacol. 16(Suppl):131T-135T.
- (11) Bitter, B. 1950. Polarography of some essential oils. Collection Czechoslov. Chem. Commun., 15:677-690.
- (12) Bitter, B. and J. Manis. 1949. Polarography of carvone and its determination in drugs and essential oils. Chem. Listy. 43:206-207.
- (13) Charlampowicz, Z. ; et al. 1966. Basic elements of home-grown vegetables. Przemysl Spozywczy. 20(1):31-35. (Pol)
- (14) Cocking, T. T. and G. Middleton. 1932. Die Bestimmung des atherischen Oles in Drogen und Gewurzen. Quart. J. Pharmac. Pharmacol. 5:521-528.

- (15) Cohn, R. 1920. Verfahren zur Herstellung eines Kaffeersatzmittels aus Dillsamen. D.R.P. 328 009.
- (16) Collett, S. 1952. Essential-oil analysis with the salicylaldehyde reaction. Mfg. Chemist. 23:96-98.
- (17) Engelland, G. C. 1969. Process for producing pickled fruit with dill. W. Ger. Pat. Applic. 1 492 650(De)
- *(17a) Essential Oil Assoc. of U.S.A.; E. O. A. No. 158, 159, 58.
- (18) Folsch, M. 1928. Über einige in Ungarn gewonnene ätherische Ole. Riechstoffind. 3: 123-125, 141-142, 162-163, 180-181.
- *(18a) Food Chemicals Codex, 1966. 1st Edition. p. 227-230.
- *(19) Friese, F. W. 1938. Zubereitungen von Dill (*Anethum graveolens* L.) als Antihäemorrhoidalia. Pharmaz. Zentralhalle Deutschland. 79:636-638.
- *(20) Ganju, K. and B. Puri. 1959. Bioflavonoids from Indian vegetables and fruits. Ind. J. Med. Res. 47:563-570.
- (21) Gerhardt, U. 1970. Routine examination of spices for volatile oils and other components. V. Herbs. Fleischwirtschaft. 50(2): 192-194, 197.
- (22) Gorokhoff, E. 1938. Die russischen ätherischen Ole. Parfum. Mod. 32: 439-447.
- (23) Grigor'yants, N. N.; et al. 1959. Ascorbic acid content in vegetables and grapes of the Turkmenian S. S. R. Izvest. Akad. Nauk Turkmen. S. S. R. 1959(5):77-80.
- (24) Grigor'yants, N. N.; et al. 1961. Characteristics of the mineral content of vegetable foods of the Turkmenian S. S. R. 1961(1): 49-53.
- *(24a) Guenther, E. 1952. Oil of Dill, p. 630-632. In E. Guenther, The Essential Oils. D. Van Nostrand Co., New York.
- (25) Gulati, B. C.; et al. 1969. Quality of seed and herb oil produced from *Anethum graveolens* L. grown in Tarai of Uttar Pradesh. Perfumery and Essential Oil Record. 60(7/8):277-281.
- *(26) Hall, R. L. 1967. Toxicants occurring naturally in spices and flavors. Nat. Acad. Sci. Nat. Res. Council. Publ. 1354:164-173.
- *(26a) Hazleton, L. W.; et al. 1956. Toxicity of Coumarin. J. Pharmacol. Exptl. Therap. 118:348.
- (27) Hoerhammer, L.; et al. 1964. New methods in teaching pharmacognosy. IX. Thin-layer chromatography of pharmaceutical Umbelliferae oils. Deut. Apotheker-Ztg. 104(40):1398-1402. (Ger)
- (28) Kalitzki, M. 1954. Investigations on the changes in the composition of the volatile oil of *Mentha piperita* L. and *Anethum graveolens* L., with special consideration of the wilting process. Pharmazie. 9(1): 61-82; (2): 155-166.

- (29) Kapelev, L. G. 1969. Accumulation of essential oil by dill plants. Maslo-Zhir. Prom. 35(7):26-27(Russ)
- (30) Karow, H. 1969. Composition and essential oils of some spices. Riechst., Aromen, Koerperpflegem. 19(2):60-66. (Ger)
- (31) Kartnig, T. 1966. Some component lipids from the fruits of *Anethum graveolens* and *Coriandrum sativum*. Fette, Seifen, Anstrichmittel. 68(2):131-134. (Ger)
- (32) Khadzhiiski, T. S. and T. V. Surlatova. 1969. Studies of the dyes in glyceride oils of Umbelliferae fruits. C. R. Acad. Bulg. Sci. 22(1): 57-60.
- (33) Khafagy, S. M. ; et al. 1968. Phytochemical investigation of the fruit of *Anethum graveolens* L. growing in Egypt. I. Examination of the volatile oil and isolation of dillapiole. Acta Pharma. Suec. 5:155-162.
- (34) Krotov, E. G. ; et al. 1971. Mixtures of quick frozen vegetables. Kholodil'naya Tekhnika. 48(2):32-33(Ru)
- (35) Lindemann, G. 1967. Umbelliferous fruits in the liqueur industry. VII. The dill. Riechst., Aromen, Koerperpflegem. 17(3):88, 90. (Ger)
- (36) Luyendijk, E. N. 1957. The formation of essential oil in Umbelliferae. Pharmaceut. Weekbld. 92(11):349-374.
- (37) Makhkamov, G. M. and Y. A. Levin. 1963. The biological role of copper and its concentration in local foods. Tr. Inst. Kraevoi Eksperim. Med., Akad Nauk Iz. SSR 1963(5):28-36.
- (38) Maruzzella, J. C. and L. Liguori. 1958. The in vitro antifungal activity of essential oils. J. Am. Pharm. Assoc., Sci. Ed. 47(4):250-254.
- *(38a) Merck Index. 1968. 8th Edition. p. 758.
- (39) Misra, K. P. and S. S. Nigam. 1969. Chemical study of essential oils from *Anethum sowa* seeds. Riechst., Aromen, Koerperpflegem. 19(5): 185-186, 189-190(Ger)
- (40) Misra, R. C. and G. S. Krishna Rao. 1961. Oxidimetric method of evaluation of volatile oils of spices. J. Sci. Ind. Res. (India) 20D:331-333.
- *(40a) Perfume and Flavor Chemicals. 1965. Items 975 and 976. S. Arc-tander.
- (41) Pospisilova, J. ; et al. 1959. Rapid modification of the method of determining provitamin A in plants. Sbornik Ceskoslov. akad. Zemel-del. ved. Rostlinnavyroba. 5:583-594.
- (42) Reilly, J. and P. J. Drumm. No year given. Bestimmung von Carvon in Dillol. Analyst. 53:209-211.
- (43) Rooma, M. Y. 1971. Contents of nitrates, nitrites and hydroxylamines in foods. Gigena i Sanitariya. 36(8):46-50.
- (44) Sadgopal. 1959. Newer potential sources of Indian essential oils. Ind. chim. belge. 24:1345-1348.

- (45) Schimmel & Co. 1928. Dillkrautöl. Ber. Schimmel. 1928:23, also 1927:25-26.
- (46) Sethi, S. 1965. Studies on chemical and economic utilization of *Anethum sowa*. Indian Perfum. 9(1):17-19.
- (47) Shah, C. C. and S. Z. Patel. 1955. Iron content of vegetables of Gujarat. Bansilal Amritlal Agr. Coll. Mag. 9(1):4-9.
- (48) Shatenshtein, V. 1970. New fish products. Rybnoe Khozyaistvo. 46(11): 51-53. (Ru)
- *(49) Shipochliev, T. 1968. Pharmacological investigation into several essential oils: First communication. Effect on the smooth Musculature. Vet. Med. Nauki. 5(6):63-69.
- (50) Soloveichik, S. I. 1946. Determination of essential oils in aqueous-alcoholic solutions and in aqueous solutions (spirits, aromatic waters, and infusions.) Zhur. Anal. Khim. 1:158-165.
- (51) Soremark, R. 1967. Vanadium in some biological specimens. J. Nutr. 92(2):183-190.
- (52) Stenlake, J. B. and W. D. Williams. 1957. Spectrophotometric determination of α , β -unsaturated aldehydes and ketones with Girard-T reagent. J. Pharm. and Pharmacol. 9:900-907.
- (53) Topalov, P. G.; et al. The composition of the fruits and the technology of extraction of essential and glyceride oils from caraway, cumin, dill, and celery. Visshiya Inst. Khranitelna Vkusova Prom. - Plodiv. 11:154-160. (Bulg)
- *(54) Truitt, Jr., E. B. ; et al. 1961. Pharmacology of Myristicin, A Contribution to the Psychopharmacology of Nutmeg. J. Neuropsychiat. 2:205.
- (55) Tschernuchin, A. 1927. Zur Frage der russischen ätherischen Öle. II. Masloboino-Shirowoje Djelo. 1927(6):13-15.
- * (56) United States Dispensatory. 1960. XXV. Part. 1. Dill. 466. J. B. Lippincott Company. Philadelphia, Pa.
- (57) Verma, S. M. 1960. Carvone analysis by ultraviolet absorption in Indian dill oils (*Anethum sowa*). Current Sci. (India) 29:345-346.
- (58) Vil'yams, V. V. and L. K. Gurinovich. 1965. A method for quantitative determination of plastoquinone in plants. Dokl. TSKhA. 109(1):143-146.
- (59) Virmani, O. P. and S. C. Datta. 1970. Essential oil of *Anethum graveolens*. (A review) Flavour Industry. 1(12):856-862.
- (60) Wisniewski, W. ; et al. 1962. Effect of physical factors on the content of essential oils in decoctions from vegetable materials. Acta Polon. Pharm. 19(5):377-382.
- (61) Zaraiskaya, E. N. and Y. G. Borisjuk. 1957. Essential oil of the seeds of dill (*Anethum graveolens*). Trudy Khar'kov. Farm. Inst. 1957(1):190-193.

Section
II

RICHARD L. HALL

Toxicants Occurring Naturally in Spices and Flavors

Although historical records are lacking, spices are certainly among the first substances, after salt, that man added to his food. These natural aromatics were seldom valued solely for their flavor, for nearly all enjoyed status as drugs, stimulants, aphrodisiacs, or food preservatives. Without much doubt, in most instances their merit lay chiefly in the mind of the user. As effective pharmacological agents became available, and our ability to assess their merits developed, the use of naturally occurring drugs, including the spices, declined. The formularies, pharmacopoeias, and dispensatories of today carry only the surviving remnants of a much larger number, and these primarily because of their use as flavors in pharmaceutical preparations.

It is not surprising that almost all our present spices are devoid of physiological effect even in amounts much greater than are normally used in food. This is partly because those few that might present some hazard have been recognized and dropped from use. Beyond this, however, is the fact that in the majority of instances, a naturally occurring toxicant in food is not only detected by taste, odor, or the common chemical sense, but it becomes distinctly unpalatable at a level several orders of magnitude below that at which toxic effects can be observed. The exceptions to this generalization form one of the reasons for this paper, and flavors contain a few of these exceptions. Even these exceptions, however, can accurately be described as self-limiting. For the purposes of this review, the substances that will be regarded as toxicants naturally occurring in flavors are those in which the customary gap, or safety factor, between levels that are organoleptically acceptable and those that are harmful is markedly narrower than usual, or the con-

SPICES

stituent
or narc
levels. S
absolut
and the
So far a
resultin
Usin
natural
probab
toxic. T
myristi
mustar
pepper
numbe

Hydro

Hydro
glycosi
oils of
glycos
pits ar
tion o

Prun
is also
While
usual
are tr
(free
and c
some
quan

RICHARD L. HALL

g Naturally

rs

ces are certainly among the
to his food. These natural
their flavor, for nearly all
siacs, or food preservatives.
their merit lay chiefly in the
cal ts became available,
doped, the use of naturally
declined. The formularies,
ay carry only the surviving
these primarily because of
parations.

resent spices are devoid of
greater than are normally
ew that might present some
from use. Beyond this, how-
ances, a naturally occurring
aste, odor, or the common
palatable at a level several
toxic effects can be observed.

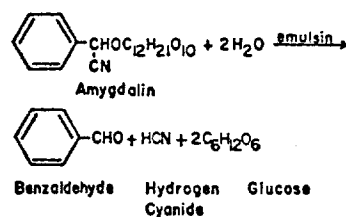
one of the reasons for this
ceptions. Even these excep-
ed as self-limiting. For the
will be regarded as toxicants
which the customary gap, or
moleptically acceptable and
wer than usual, or the con-

stituent in question exhibits unusual features of toxicity, such as vesicant or narcotic action, carcinogenesis, or toxicity at extraordinarily low levels. Since toxicity, the capacity of a substance to cause harm, is an absolute property, there is a hazard only if the state of the organism and the conditions and levels of use permit this capacity to be realized. So far as spices and flavors are concerned, the examples of actual harm resulting from their ingestion are so rare as to be medical curiosities.

Using these general criteria, there are eight substances that occur naturally in flavoring materials in current or recent use that would probably be included in any list of substances generally regarded as toxic. These are: hydrogen cyanide, found in a number of glycosides; myristicin, in mace, nutmeg, and dill; allyl isothiocyanate, in brown mustard; umbellulone, in California bay laurel; capsaicin, in red pepper; and coumarin, safrol, and thujone, each of which occurs in a number of different species.

Hydrogen Cyanide

Hydrogen cyanide (HCN) occurs bound chemically in a number of glycosides found in food. Oil of bitter almonds, a generic name for the oils of bitter almonds, apricot kernels, or peach kernels, contains the glycoside amygdalin. The enzyme emulsin is also present, and when the pits are crushed and moistened, the glycoside is cleaved with the liberation of hydrogen cyanide (Reaction 1). The leaves of the cherry laurel,



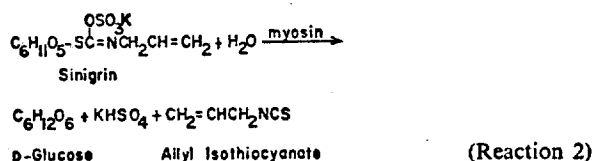
(Reaction 1)

Prunus laurocerasus L., contain a similar glycoside, prulaurasin, which is also split by emulsin to release benzaldehyde and hydrogen cyanide. While such oils may originally contain up to 11 percent of HCN, the usual level is 2–4 percent.¹ All oils produced commercially for food use are treated chemically to remove the HCN and are designated FFPA (free from prussic acid). Homemade foods containing these materials, and other natural sources of hydrogen cyanide such as cashew nuts and some brandies, result in the continued consumption of insignificant quantities of the toxicant. Considerable evidence shows that the body

can eliminate small quantities of cyanide, both by conversion to the much less toxic thiocyanate and by combination with cystine. These metabolic routes appear to be capable of handling any quantities ingested from natural dietary sources, but not the abnormal amounts from environmental or nonfood hazards.²

Allyl Isothiocyanate

Brown mustard, *Brassica juncea* (L.) Coss., contains the glycoside sinigrin and the enzyme myosin. When the seeds are moistened and crushed, glucose, potassium bisulfate, and allyl isothiocyanate result (Reaction 2). Allyl isothiocyanate is a potent irritant; its usefulness as a



local counterirritant accounts for the listing of mustard in the *U.S. Dispensatory*. Allyl isothiocyanate has been isolated from horseradish,^{3,4} several other members of the genus *Brassica*, a large group that includes mustard, broccoli, and cabbage, and also from rocket salad, *Eruca sativa*.⁵ Although experience in human use is extensive, the literature reports of toxicological data are relatively meager, and simply confirm that in high concentration allyl isothiocyanate is a strong irritant. Rusch *et al.* report an increase in mitotic activity after a single application to mouse ears.⁶ Not surprisingly, Cordier and Cordier found it toxic on intravenous injection.⁷

Umbellulone

The leaves of the California bay laurel tree (*Umbellularia californica* Nutt.) have had considerable past food use, especially for seasoning game. They contain from 0.5 to 4 percent of an irritating oil, of which the major constituent, accounting for from 40 to 60 percent, is umbellulone (I). According to Guenther,⁸ care is advisable to avoid injury while collecting the branches. Drake and Stuhr⁹ mention that proximity to the oil or its vapors has resulted in severe headache, skin irritation, and in some cases unconsciousness. They found umbellulone to produce a decided hemolysis *in vivo* and compared its effects on the nerves and

fibers of frog heart with the depressant, acting in parallel. Because other spices, including *fenugreek* (*Trigonotis nobilis* L.), are available and has no currently recognized

Capsaicin

The substance responsible for the genus *Capsicum*, the It is a highly irritating substance 1:1,000,000. Applied in contact with Anyone who has had occasional experience familiar with its ability to cause irritations and increased gastric secretions from the direct effect of the membranes of the mouth

Myristicin

Nutmeg and mace (bo from 8 to 15 percent of XVI as Myristica Oil. A only physiologically act number of members of parsley,¹⁴ celery,¹⁵ and c goes back at least to th probably earlier in India

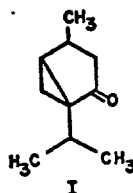
conversion to the
with cystine. These
g any quantities in-
abnormal amounts

contains the glycoside
are moistened and
isothiocyanate result
et; its usefulness as a

(Reaction 2)

mustard in the U.S.
solanaceae from horse-
assica, a large group
and also from rocket
man use is extensive,
relatively meager, and
isothiocyanate is a
mitotic activity after a
singly, Cordier and

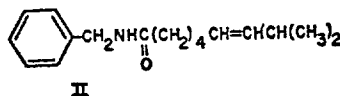
umbellularia californica
specially for seasoning
irritating oil, of which
50 percent, is umbel-
sable to avoid injury
ention that proximity
ache, skin irritation,
umbellulone to produce
ects on the nerves and



fibers of frog heart with those of atropine. They concluded that it was a depressant, acting in part by blocking of pulmonary circulation. Because other spices, including the traditional bay or laurel (*Laurus nobilis* L.), are available without this hazard, the California bay laurel has no currently recognized status as an appropriate food ingredient.

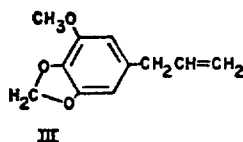
Capsaicin

The substance responsible for the heat, or pungency, of all members of the genus *Capsicum*, the red peppers, is the amide capsaicin (II).^{10,11} It is a highly irritating substance, detectable in water at dilutions of over 1:1,000,000. Applied in concentrated form to the skin, it is a vesicant. Anyone who has had occasion to consume foods high in capsaicin is familiar with its ability to induce sweating and salivation. These reactions and increased gastric flow are apparently reflex actions resulting from the direct effect of capsaicin on the pain fibers in the mucous membranes of the mouth.^{12,13}



Myristicin

Nutmeg and mace (both from *Myristica fragrans* Houtt.) contain from 8 to 15 percent of a volatile oil, which was still listed in U.S.P. XVI as Myristica Oil. About 4 percent of the oil is myristicin (III), its only physiologically active ingredient. Myristicin is also found in a number of members of the carrot family (Umbelliferae), including parsley,¹⁴ celery,¹⁵ and dill.¹⁶ The medicinal use of nutmeg and mace goes back at least to the early Middle Ages in the Arab world, and probably earlier in India. Then, these spices enjoyed high esteem as a



treatment for a wide variety of conditions including toothache, dysentery, cholera, rheumatism, halitosis, and skin diseases. Western medicine followed this lead, and improved upon it, until nutmeg came to be thought of as almost a panacea. Disenchantment did not set in until the nineteenth century, during which their scope of application was narrowed sharply. At about this time, however, nutmeg acquired in some unknown way the reputation of being an emmenagogue and abortifacient. This wholly unjustified reputation persists even today and is responsible for a number of cases of nutmeg poisoning.¹⁷ Taken in large quantity, nutmeg and mace exhibit pronounced narcotic and psychomimetic properties, somewhat comparable to alcoholic intoxication.¹⁸ A puzzling aspect of their action is that the effects of the spice are greater than those of an equivalent amount of myristicin, even though the myristicin is the only constituent that separately causes significant physiological response. Very high doses may result in liver damage or death. During the last century, awareness of the narcotic properties of nutmeg led to occasional instances of use for this purpose. Nutmeg is the spice usually chosen for the practical reason that it is cheaper and more readily available. The dosage ordinarily involved in attempts at narcotic or abortifacient use are of the order of two whole nutmegs, or an ounce of the grated product—a quantity far in excess of any conceivable flavor use. There is little evidence that those who try the use of nutmeg as a narcotic indulge in much repetition; the side effects and aftereffects, including headache, cramps, and nausea, are reported to be common, severe, and extremely unpleasant.

Truitt *et al.*¹⁸ advance the supposition that myristicin acts as a weak monoamine oxidase inhibitor. If it follows a metabolic pathway similar to that of safrol (q.v.), it might well be converted *in vivo* into substances similar to or identical with known psychomimetic agents such as 3-methoxy-4,5-methylenedioxyamphetamine.¹⁷

Coumarin

Coumarin (IV) is found widely distributed in a number of substances that are natural sources of flavors. While neither it nor its principal natural source, tonka beans [*Dipteryx odorata* (Aubl.) Willd.] are now

used in food, it is an important constituent of *farnesiana* (L.) Willd. lovage, *Levisticum officinale*;²³ *Copaifera* (Walt.) Cass.;²⁵ and v. and lovage are used woodruff is the principal

Coumarin, used as in reports, initially extensive liver damage high levels. Prior to imitation vanilla flavor.

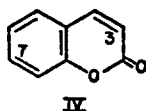
Coumarin is metabolized in various positions, followed by acid, and elimination

Safrol

One of the most widely used now regarded as toxic (100%) of the oil of sassafras

(Nutt.) Nees.³⁰ It is found in *momum micranthum* varieties.^{31,32} It is also found in ginger,³⁴ California

In toxicological studies, the Drug Administration has reported the administration of safrol as causing tumors, and that lo-



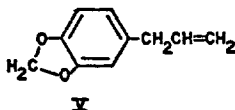
used in food, it is an important flavoring constituent of cassie, *Acacia farnesiana* (L.) Willd.;¹⁹ lavender, *Lavandula officinalis* Chaix;^{20,21} lovage, *Levisticum officinale* Koch;²² yellow sweet clover, *Melilotus officinalis*;²³ *Copaifera lansdorfii*;²⁴ deer tongue, *Trilisa odoratissima* (Walt.) Cass.;²⁵ and woodruff, *Asperula odorata* L.²⁶ Cassie, lavender, and lovage are used rather widely in candy and liqueur flavors, and woodruff is the principal flavor of May wine.

Coumarin, used as such, disappeared from flavor use in 1954 following reports, initially by Hazleton *et al.*²⁷ and later by Sporn,²⁸ of extensive liver damage to rats resulting from the feeding of relatively high levels. Prior to that time, it was widely used as an ingredient of imitation vanilla flavors.

Coumarin is metabolized largely by hydroxylation at the 3 and 7 positions, followed by conjugation with glucuronic acid or sulfuric acid, and elimination of the conjugate.²⁹

Safrol

One of the most widespread of the essential oil constituents that are now regarded as toxic is safrol (V). It is the major constituent (85 percent) of the oil of sassafras, the oil of the root bark of *Sassafras albidum*



(Nutt.) Nees.³⁰ It forms 95 percent of micranthum oil, from *Cinnamomum micranthum* Hayata, and occurs in several related species and varieties.^{31,32} It is also found in mace and nutmeg,³³ Japanese wild ginger,³⁴ California bay laurel,³⁵ and a number of other species.

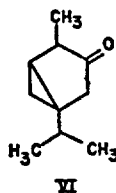
In toxicological studies carried out by the United States Food and Drug Administration, Lehman reported³⁶ that the continuous administration of safrol at high levels in the total diet of rats caused liver tumors, and that lower levels produced lesser noncancerous damage.

Although the evidence suggested that a low safe level of use could be established, safrol and those oils of which it is the major constituent have been dropped from use because of the provision of the Food Additives Amendment of 1958 excluding from use in food, substances which, in the diet of man or experimental animals, are found to cause cancer.

Little metabolic work has been done, but piperonylic acid has been found to be a metabolite of safrol and isosafrol after administration to dogs.³⁷

Thujone

The flavor constituent that first gained toxicological notoriety is thujone (VI). It is a major component of oil of wormwood, *Artemisia absinthium* L., the principal flavoring ingredient of the liqueur



absinthe.³⁸ Serious physiological consequences resulting from the excessive use of this beverage, particularly in France, led to a campaign that resulted in its abolition there in 1915. Wormwood continues to be used in trace quantities in flavored wines such as vermouth. Toxicity studies have shown that, in sufficient quantity, thujone produces convulsions associated with lesions of the cerebral cortex.³⁹⁻⁴¹ Thujone occurs in two stereoisomeric forms one of which is called α , *l*, or (–) thujone, and the other β , *d*, or (+) isothujone. Both thujones occur in several species of the genus *Artemisia*.⁴²⁻⁴⁵ Both forms are present in oil of wormwood and in oak moss, *Evernia prunastri* (L.) Ach. and *E. furfuracea* (L.) Mann.⁴⁶ The α form is the major constituent of cedar leaf oil (oil of thuja), from *Thuja occidentalis* L.,^{47,48} and is an important component of sage, *Salvia officinalis* L.,^{49,50} Tansy, *Tanacetum vulgare* L., contains the β form,^{51,52} as does yarrow, *Achillea millefolium* L.⁵³

Little is known of the metabolism of thujone. In the rabbit, at least a portion may be converted by hydroxylative cleavage of the bridge link to the tertiary alcohol and excreted as the glucuronide.⁵⁴

One cannot avoid noting the relationship between myristicin and thujone. At this stage of our knowledge, the connections between these relationships lack the physiological effect.

It is now evident that the occurrence of thujone to a single species, thujone, are found, at least in different genera, but only in some to indicate, in several cases summarized here. As more studies are made of the components of essential oils, it is expected to find that thujone is nearly ubiquitous, and that it has a remarkable capacity of being detected with small quantities of

REFERENCES

1. E. Guenther, *The Essential Oils*, 390.
2. R. T. Williams, *Detoxification*, 390.
3. A. Guillaume, "Horse-..."
4. G. Janiček and A. Čížek, *Potravin*, 5, 204 (1954).
5. A. Mohammad and S. ... Species and *Eruca sativa*.
6. H. P. Rusch, D. Bosc, "Mitotic Activity and ... Intern. Contra Cancerur..."
7. D. Cordier and G. C... the Cardiovascular S... Compt. Rend. Soc. Bio...
8. E. Guenther, *The Essential Oils*.
9. M. E. Drake and E. T... ties of Umbellulone."
10. H. Pella de la Flor, "Intest," *Anales Fac. (Lima)*, 5, 206 (1954).
11. M. Nuñez-Samper, "in Capsicum," *Anales*.
12. C. C. Toh, T. S. Le... Capsaicin and Analog

safe level of use could be it is the major constituent the provision of the Food from use in food, substances animals, are found to cause

at piperonylic acid has been safrol after administration to

toxicological notoriety is oil of wormwood, *Artemisia* ingredient of the liqueur

quences resulting from the y in France, led to a cam- 1915. Wormwood continues ed wines such as vermouth. cient quantity, thujone pro- s of the cerebral cortex.³⁹⁻⁴¹ rms one of which is called +) isothujone. Both thujones *Artemisia*.⁴²⁻⁴⁵ Both forms are moss, *Evernia prunastri* (L.) e α form is the major con- om *Thuja occidentalis* L.,^{47,48} *Salvia officinalis* L.^{49,50} Tansy, ^{51,52} as does yarrow, *Achillea* thujone. In the rabbit, at least a ve cleavage of the bridge link e glucuronide.⁵⁴

One cannot avoid noting the close relationship in chemical structure between myristicin and safrol and between thujone and umbellulone. At this stage of our knowledge, it would be risky to draw conclusions from these relationships, since other substances equally closely related lack the physiological effects of those discussed here.

It is now evident that while some substances are limited in known occurrence to a single species, others, such as coumarin, safrol, and thujone, are found, at least in traces, in species not merely of several different genera, but of quite unrelated families. Unpublished data indicate, in several cases, far broader distribution than that summarized here. As more sensitive methods of separating and identifying the components of essential oils are developed and applied, one may expect to find that at least some of these relatively toxic materials are nearly ubiquitous, and that we must continue to rely upon the remarkable capacity of the human body to deal promptly and effectively with small quantities of toxic materials.

REFERENCES

1. E. Guenther, *The Essential Oils*, Van Nostrand, New York (1952), Vol. 5, p. 52.
2. R. T. Williams, *Detoxication Mechanisms*, 2nd ed., Wiley, New York (1959), p. 390.
3. A. Guillaume, "Horse-radish and Its Applications," *Prod. Pharm.*, 6, 383 (1951).
4. G. Janíček and A. Čapek, "Volatile Phytoncide of Horse-radish," *Prumysl Potravin*, 5, 204 (1954).
5. A. Mohammad and S. Ahmad, "A Note on Essential Oil of Mustard in *Brassica* Species and *Eruca sativa*," *Indian J. Agr. Sci.*, 15, 181 (1945).
6. H. P. Rusch, D. Bosch, and R. K. Boutwell, "The Influence of Irritants on Mitotic Activity and Tumor Formation in Mouse Epidermis," *Acta Unio Intern. Contra Cancrum*, 11, 699 (1955).
7. D. Cordier and G. Cordier, "Mode of Action of bis(2-Chloroethyl) Sulfide on the Cardiovascular System; Effects of Chemically Similar Compounds," *Compt. Rend. Soc. Biol.*, 145, 1310 (1951).
8. E. Guenther, *The Essential Oils*, Van Nostrand, New York (1950), Vol. 4, p. 207.
9. M. E. Drake and E. T. Stuhr, "Some Pharmacological and Bactericidal Properties of Umbellulone," *J. Am. Pharm. Assoc. Sci. Ed.*, 24, 196 (1935).
10. H. Pella de la Flor, "Chemical Study of *Capsicum frutescens*. Capsaicine Content," *Anales Fac. Farm. Bio-Quim., Univ., Nucl. Mayor San Marcos (Lima)*, 5, 206 (1954).
11. M. Nuñez-Samper, "Capsaicin, Its Content and Colorimetric Determination in Capsicum," *Anales Bromatol. (Madrid)*, 3, 323 (1951).
12. C. C. Toh, T. S. Lee, and A. K. Kiang, "The Pharmacological Actions of Capsaicin and Analogs," *Brit. J. Pharmacol.*, 10, 175 (1955).

13. J. Pórszász, L. Gyorgy, and K. Gibiszer-Pórszász, "Cardiovascular and Respiratory Effects of Capsaicin," *Acta Physiol. Acad. Sci. Hung.*, **8**, 60 (1955).
14. J. Small, "Parsley Seed," *Food*, **18**, 268 (1949).
15. M. Karmazin, "Critical Examination of Celery Fruit and Root on the Basis of a Colorimetric Determination of Apiol and Myristicin," *Pharmazie*, **10**, 57 (1955).
16. *Ann. Rept.*, Schimmel & Co. (1927), pp. 36-37.
17. A. T. Weil, "Nutmeg as a Narcotic," *Econ. Botany*, **19**, 194 (1965).
18. E. B. Truitt, Jr., E. Callaway III, M. C. Braude, and J. C. Krantz, Jr., "Pharmacology of Myristicin, A Contribution to the Psychopharmacology of Nutmeg," *J. Neuropsychiat.*, **2**, 205 (1961).
19. D. La Face, "The Concrete Essence of *Acacia farnesiana*," *Helv. Chim. Acta*, **33**, 249 (1950).
20. C. Kleber, "Acetates in Oil of Lavender," *Am. Perfumer*, **21**, 680 (1927), and a letter of comment by A. St. Pfau, *Am. Perfumer Essent. Oil Rev.*, **22**, 275 (1927).
21. C. F. Seidel, H. Schinz, and P. H. Müller, "Lavender Oil. III. Monoterpene Alcohols and Acids Occurring as Esters in French Lavender Oil," *Helv. Chim. Acta*, **27**, 663 (1944).
22. Y. R. Naves, "Volatile Plant Materials. XXIV. Composition of the Essential Oil and Resinoid of Lovage Root," *Helv. Chim. Acta*, **26**, 1281 (1943).
23. J. M. Slatensk, "Some Causes for Variation of Coumarin Content in Sweet Clover," *J. Am. Soc. Agron.*, **39**, 596 (1947).
24. W. B. Mors and H. J. Monteiro, "Two Coumarins in the Seed of *Copaifera langsdorffii*," *Anais Assoc. Brasil. Quim.*, **18**, 181 (1959).
25. A. Osol and G. E. Farrar, Jr., eds., *The Dispensatory of the United States of America*, 25th ed., Lippincott, Philadelphia, Pa. (1955), p. 398.
26. *The Merck Index*, 7th ed. Merck & Co., Rahway, N.J. (1960), p. 1105.
27. L. W. Hazleton, T. W. Tusing, B. R. Zeitlin, R. Thiessen, Jr., and H. K. Murer, "Toxicity of Coumarin," *J. Pharmacol. Exptl. Therap.*, **118**, 348 (1956).
28. A. Sporn, "Toxicity of Coumarin as a Flavoring Agent," *Igiene*, **9**, 121 (1960).
29. R. T. Williams, *Detoxication Mechanisms*, 2nd ed., Wiley, New York (1959), p. 628.
30. M. R. Dodsworth, "Some Considerations on Sassafras Oil," *Bol. Divulgação Inst. Oleos. No. 3*, 21 (1945).
31. E. Guenther, *The Essential Oils*, Van Nostrand, New York (1950), Vol. 4, p. 280.
32. T. Naito, "The Constituents of the Volatile Oil from the Leaf of *Cinnamomum camphora* var. *glaucescens*," *J. Chem. Soc. Japan*, **64**, 1125 (1943).
33. F. B. Power and A. H. Solway, "The Constituents of the Essential Oil of Nutmeg," *J. Chem. Soc.*, **91**, 2037 (1907).
34. T. Harada and Y. Saiki, "Pharmaceutical Studies of Japanese Wild Ginger. II. Paper Chromatography of Essential Oils," *Pharm. Bull. (Tokyo)*, **4**, 223 (1956).
35. F. B. Power and F. H. Lees, "The Constituents of the Essential Oil of Californian Laurel," *J. Chem. Soc.*, **85**, 629 (1904).
36. A. J. Lehman, "Report on Safrole," *Assoc. Food Drug Officials U.S., Quart. Bull.*, **25**, 194 (1961).
37. R. T. Williams, *Detoxication Mechanisms*, 2nd ed., Wiley, New York (1959), p. 371.
38. P. Balavoine, "Thujone in Absinth and Its Imitations," *Mitt. Gebiete Lebensm. Hyg.*, **43**, 195 (1952).

"Cardiovascular and Respiratory," *Hung.*, 8, 60 (1955).

fruit and Root on the Basis of a
"Histidine," *Pharmazie*, 10, 57

19, 194 (1965).

J. C. Krantz, Jr., "Pharmacology of Nutmeg,"

"nesiana," *Helv. Chim. Acta*,

"fumer," 21, 680 (1927), and a

"ent. Oil Rev.", 22, 275 (1927).

ender Oil. III. Monoterpene
Lavender Oil," *Helv. Chim.*

Composition of the Essential
Oil, 26, 1281 (1943).

Coumarin Content in Sweet

ins in the Seed of *Copaifera*
59).

ator, the United States of
55), p. 398.

J. (1960), p. 1105.

Thiessen, Jr., and H. K.
l. *Therap.*, 118, 348 (1956).

gent," *Igiene*, 9, 121 (1960).

Wiley, New York (1959),

afra Oil," *Bol. Divulgação*

W York (1950), Vol. 4, p. 280.

om the Leaf of *Cinnamomum*
1125 (1943).

ents of the Essential Oil of

of Japanese Wild Ginger. II.

Bull. (Tokyo), 4, 223 (1956).

of the Essential Oil of Cali-

Drug Officials U.S., Quart.

Wiley, New York (1959),

ns," *Mitt. Gebiete Lebensm.*

39. F. H. Pike, M. Osnato, and J. Notkin, "The Combined Action of Some Convulsant Agents in Small Doses and the Action of Bromides in Experimentally Induced Convulsions," *Arch. Neurol. Psychiat.*, 25, 1306 (1931).
40. H. M. Keith and G. W. Stavaky, "Experimental Convulsions Induced by Administration of Thujone. A Pharmacologic Study of the Influence of the Autonomic Nervous System on These Convulsions," *Arch. Neurol. Psychiat.*, 34, 1022 (1935).
41. L. Oppen, "Pathologic Picture of Thujone and Monobromated Camphor Convulsions: Comparison with Pathologic Picture of Human Epilepsy," *Arch. Neurol. Psychiat.*, 41, 460 (1939).
42. M. I. Goryaev, I. M. Shabanov, and L. A. Ignatova, "Essential Oil of *Artemisia mogoltavica*," *Izv. Akad. Nauk Kaz. SSR, No. 123, Ser. Khim.*, No. 7, 75 (1953).
43. M. I. Goryaev and Zh. K. Gimaddinov, "Essential Oil of *Artemisia rutaefolia*," *Zh. Prikl. Khim.*, 32, 1878 (1959).
44. M. I. Goryaev and E. I. Satdarova, "Analysis of the Essential Oil of *Artemisia serotina*," *Tr. Inst. Khim. Nauk, Akad. Nauk Kaz. SSR*, 4, 37 (1959).
45. L. K. Tikhonova and M. I. Goryaev, "The Chemical Composition of the Essential Oil from *Artemisia jerganensis*," *Izv. Akad. Nauk Kaz. SSR, Ser. Khim.*, No. 2, 65 (1957).
46. A. St. Pfau, "Composition of Commercial Oakmoss Products," *Riechstoffe ind. Kosmetik*, 12, 179, 208 (1937).
47. E. Jahns, "Über das ätherische Oel von *Thuja occidentalis*," *Arch. Pharm.*, 221, 748 (footnote) (1883).
48. O. Wallach, "Zur Kenntniss der Terpene und der ätherischen Oele," *Ann. Chem.*, 272, 99 (1893).
49. N. Vernazza, "Thujone in Dalmation Sage Oil," *Acta Pharm. Jugoslav.*, 7, 163 (1957).
50. C. H. Brieskorn and E. Wenger, "Constituents of *Salvia officinalis*. XI. The Analysis of Ethereal Sage Oil by Means of Gas and Thin-Layer Chromatography," *Arch. Pharm.*, 293, 21 (1960).
51. H. Braun, "Effect of Extracts from *Tanacetum vulgare* on Gastric Secretion," *Med. Monatsschr.*, 3, 528 (1949).
52. Ya. Maizite, A. Klyava, and L. Kluga, "Composition and Anthelmintic Action of Tansy," *Latvijas PSR Zinatnu Akad., Kim. Inst. Zinatniskie Raksti*, 1, 101 (1950).
53. R. E. Kremers, "The Chemistry of the Volatile Oil of Milfoil. A Study of the Application of Modern Organic Chemistry to Drug Plant Investigations," *J. Am. Pharm. Assoc.*, 10, 252 (1921); "Oil of *Achillea millefolium*, L. 1922," *J. Am. Pharm. Assoc.*, 14, 399 (1925).
54. R. T. Williams, *Detoxication Mechanisms*, 2nd ed., Wiley, New York (1959), p. 530.

butyryl chloride. The acid chloride (1.2 g.) was dissolved in acetone (7.5 ml.) and added dropwise (10 min.) to a cooled (ice-bath) solution of sodium azide (0.91 g.) in water (7.5 ml.). When the addition was complete, the temperature of the mixture was allowed to rise to 15° and the mixture was rapidly stirred for 30 min. The upper (organic) layer was carefully separated and added dropwise to benzene (20 ml.) at 60°. The benzene solution was maintained at this temperature for 1 hr. and added to dried ether (1 l.) containing finely ground 2,4-dinitrophenylhydrazine (1.0 g.). The mixture was vigorously refluxed for 3 hr. after which time a small amount of (red) undissolved starting material

was filtered off. The solution was set aside overnight and a yellow solid separated (0.62 g., 42%). Recrystallisation from aqueous ethanol gave 1-(2,4-dinitrophenyl)-4-(1-methylpropyl)semicarbazide, m. p. 220°, identical (mixed m. p., infrared spectra) with the material prepared by method (a). The semicarbazide prepared by route (b) had $[\alpha]_{D}^{25} = 37.0^\circ$ (c 1 in acetic acid).

State Maintenance Grants for Research (to A. F. H. and J. B. A.) are gratefully acknowledged.

[7/633 Received, May 22nd, 1967]

The Constituents of Native Umbelliferae. Part I. Coumarins from Dill (*Anethum graveolens* L.)

By R. T. Aplin and C. B. Page, The Dyson Perins Laboratory, Oxford University

Scopoletin and a new coumarin, 6,7-dihydro-8,8-dimethyl-2*H*,8*H*-benzo[1,2-*b*:5,4-*b'*]dipyrans-2,6-dione, have been isolated from the upper parts of dill. The n.m.r. and mass spectra of these compounds and their transformation products are described.

DILL (*Anethum graveolens*) a herb growing in Southern England has been known for its medicinal properties since Anglo-Saxon times.¹ The steam volatile oil has been the subject of a considerable number of investigations.² During the examination of native umbelliferae for acetylenic³ and terpenoid constituents a number of intensely ultraviolet-fluorescent spots were observed upon t.l.c. examination of the ether extracts of various species.

Extracts of the upper parts of Dill (*Anethum graveolens*) grown locally, displayed intense ultraviolet

dipyrans-2,6-dione] $C_{14}H_{12}O_4$,* m. p. 177.5–178°, showed ν_{\max} 1751 (α,β -unsaturated δ -lactone); 1297, 822 (conjugated *cis*-CH=CH); 1143 cm^{-1} (C–O–C) typical of many coumarins and an aryl ketone (ν_{\max} 1698 cm^{-1}). The n.m.r. spectrum (Table I) is consistent with the structure (I), the isomeric structure (II) being rejected on the grounds that the aromatic proton at τ 2.01 is at too low a field to have an oxygen substituent on an adjacent carbon atom.⁴ This was confirmed by the isolation of resorcinol on fusion with potassium hydroxide. Furthermore, the ultraviolet absorption spectrum re-

TABLE I
Chemical shifts (τ) for compounds (I) and (IV)–(VIII)

Compound	3-H	4-H	5-H	6-H	7-H	8-H	10-H	H(OH)	H(OMe)	H(OMe)	$J_{3,4}$ (c./sec.)	$J_{6,7}$ (c./sec.)
(I)	3.71(d)	2.33(d)	1.99(d)		7.23(s)		3.19(s)			8.50(s)	9.4	
(IV)	3.96(d)	2.51(d)	2.48(s)	5.15(q)*	7.95(dq)†		3.45(s)	7.12		8.61(d)		
(V)	4.34(d)	2.42(d)	2.96(s)	3.65(d)	3.81(d)		3.27(s)			8.54(s)	9.8	9.4
(VI)	3.68(d)	2.40(d)	3.07(s)			3.14(s)		3.85(s)	6.05(s)		9.4	
(VII)	3.72(d)	2.40(d)	3.03(s)			3.17(s)		4.37(s)	6.02(s)		9.3	
(VIII)	3.72(d)	2.40(d)	3.14(s)			3.14(s)			6.05(s)		9.4	
									6.08(s)			

s = Singlet, d = doublet, q = quartet, dq = double quartet.

* Quartet on D_2O exchange. † $J_{AB} = 13.2$; $J_{AX} = 6.4$; $J_{BX} = 9.4$ c./sec.

absorption λ_{\max} 3425, 3300, 3070, 2980, and 2545 Å and exhibited two major intense ultraviolet fluorescent spots on t.l.c. examination (R_F 0.44 and 0.09). Chromatography on silica gel afforded two crystalline compounds. The major constituent [(I) R_F 0.44; 6,7-dihydro-8,8-dimethyl-2*H*,8*H*-benzo[1,2-*b*:5,4-*b'*]-

* The compositions of the molecular ion and major fragments were determined by high resolution measurements.

¹ F. Ransonin, 'British Herbs,' Pelican Books A183, Penguin Books Ltd., London, 1949, p. 157.

² E. Guenther, 'The Essential Oils,' D. Van Nostrand & Company Inc., New York, 1950, p. 630.

sembles closely that reported for the monomethyl ether of clausenin (III).⁵

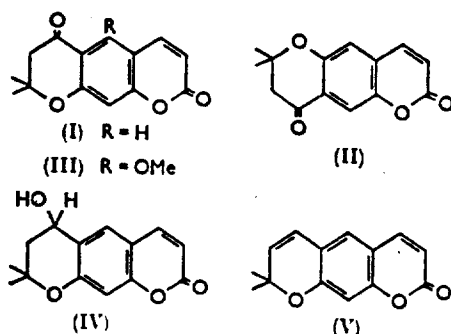
Reduction of (I) with sodium borohydride afforded the benzylic alcohol (IV), the n.m.r. spectrum of (IV) (Table I) indicated that the reduction had proceeded to give exclusively the equatorial alcohol [(IVa) Figure 1].

³ Sir Ewart R. H. Jones, S. Safe, and V. Thaller, *J. Chem. Soc. (C)*, 1966, 1220.

⁴ J. B. Bredenberg and J. N. Schoolery, *Tetrahedron Letters*, 1961, 285.

⁵ B. S. Jashi and V. N. Kamat, *Tetrahedron Letters*, 1966, 5767.

The proton at C-6 appears as the X part of an ABX pattern with $J_{AX} = 9.4$ c./sec., $J_{BX} = 6.4$ c./sec. The



calculated values, based on a Karplus equation modified for pyran ring systems,⁶ for the two alcohols shown in

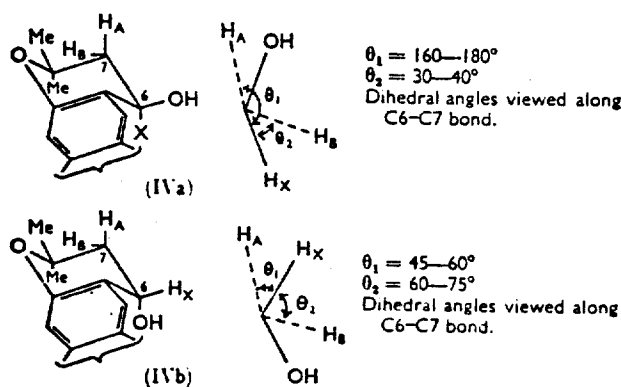


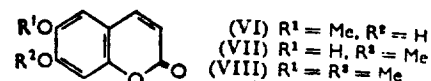
FIGURE 1

Figure 1 are for (IVa) $J_{AX} = 9-10$ c./sec. $J_{BX} = 5-6$ c./sec., and for (IVb) $J_{AX} = 2-4$ c./sec. $J_{BX} = 1-2$

by the line broadening of the signals at τ 8.08 and 8.12 (quartet) due to these protons.

Dehydration of (IVa) with toluene-*p*-sulphonic acid afforded xanthyletin (V),⁷ confirming the assigned structure (I).

The second crystalline constituent (R_f 0.09) had physical constants identical to those reported for scopoletin (VI).⁸



This conclusion was strongly supported by its mass spectrum which exhibited an intense $M - 15$ fragment (Table 2) expected for a 6-methoxycoumarin⁹ in contrast

TABLE 2

Major fragments in the mass spectra of the methyl ethers of 6,7-dihydroxycoumarin

Compound	M^+		g		h		i	
	m/e	(%)	m/e	(%)	m/e	(%)	m/e	(%)
(VI)	192	100	177	52	164	17	149	26
(VII)*	192	100	191	5	164	40	163	3
(VIII) ¹⁰	206	100	191	46	178	27	163	33†

Compound	i'		j		j'	
	m/e	(%)	m/e	(%)	m/e	(%)
(VI)	121	9	135	2	121	14
(VII)*	149	53	135	2	121	14
(VIII) ¹⁰	135	22‡				

* $M - 15$ m/e 177, 11%. † $(i + i')$. ‡ $(j + j')$.

to the weak $M - 15$ fragment (Table 2) observed for the isomeric compound (VII). Slight differences were also observed in the n.m.r. spectra of (VI) and (VII) (see Table 1). Methylation with diazomethane afforded 6,7-dimethoxycoumarin (VIII)¹⁰ identical in all respects

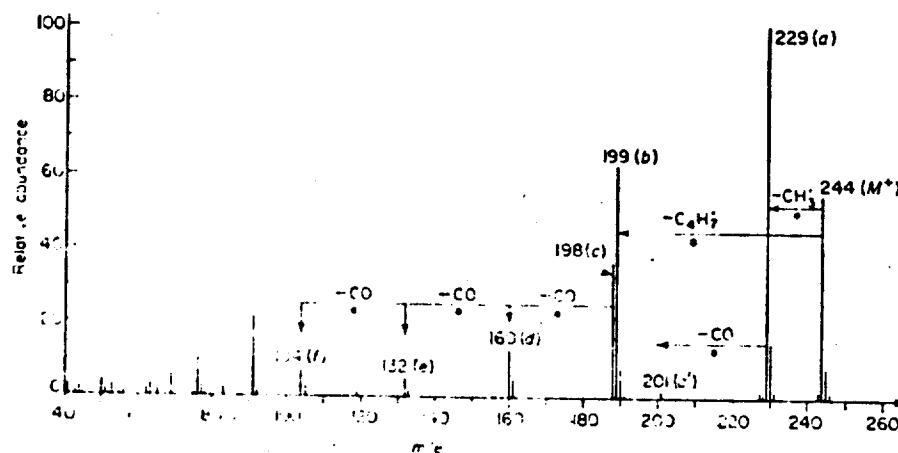


FIGURE 2 Mass spectrum of (I, R = H)

c./sec. The axial C-8 methyl group is also coupled ($J = ca. 1$ c./sec.) to the axial C-7 proton (H_A) as shown

with an authentic sample obtained by the hydrolysis and subsequent methylation of aesculin.¹¹

* L. K. O'Neill, Ph.D. Thesis, University of Alberta, Edmonton, 1966.

† F. E. King, J. R. Housley, and T. J. King, *J. Chem. Soc.*, 1954, 1392.

‡ W. B. Moss and D. Ribeiro, *J. Org. Chem.*, 1957, 22, 978.

§ C. Djerassi and R. Shapiro, *J. Org. Chem.*, 1965, 30, 955.

|| R. Seka and P. Kallir, *Chem. Ber.*, 1931, 64, 909.

11 F. von Rohleder and R. Schwarz, *Annalen*, 1853, 87, 186.

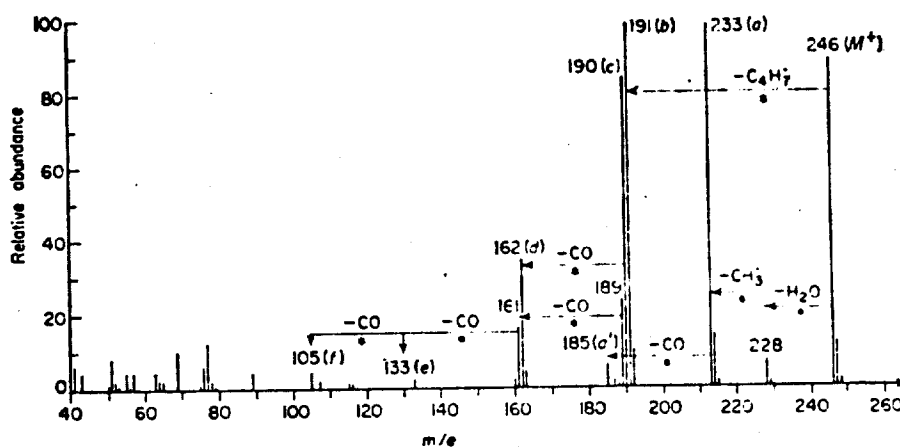
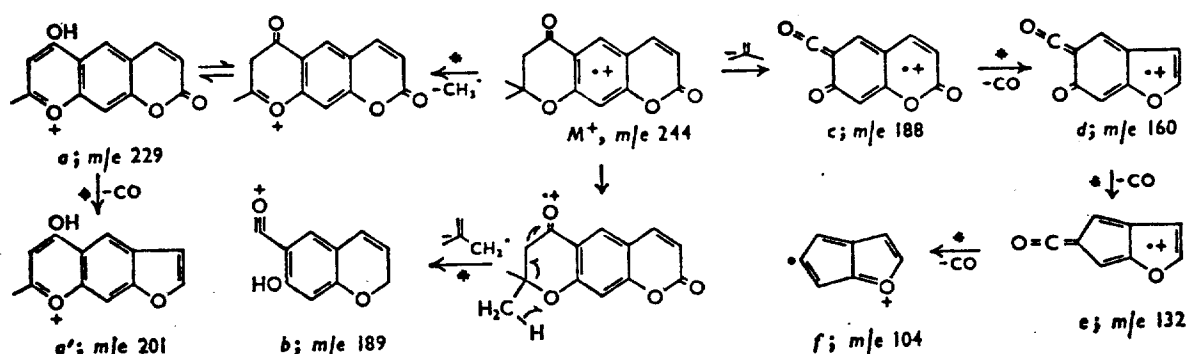


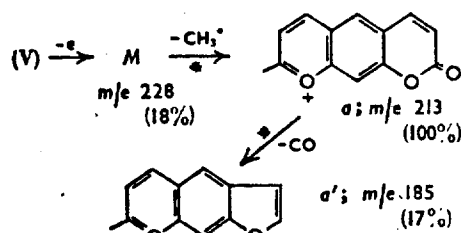
FIGURE 3 Mass spectrum of (IV) (metastable peaks were also observed for the following transitions: $191 \xrightarrow{-H^+} 190$; $190 \xrightarrow{-H^+} 189$; $162 \xrightarrow{-H^+} 161$)



Scheme 1

* Metastable peak observed

Mass Spectra.—The mass spectra of (I) and (IV) (Figure 2 and 3) exhibit the characteristic fragmentations of coumarins,¹² dimethylchromenes,¹³ and chroman-4-ones.¹³ Ions resulting from fragmentation of the



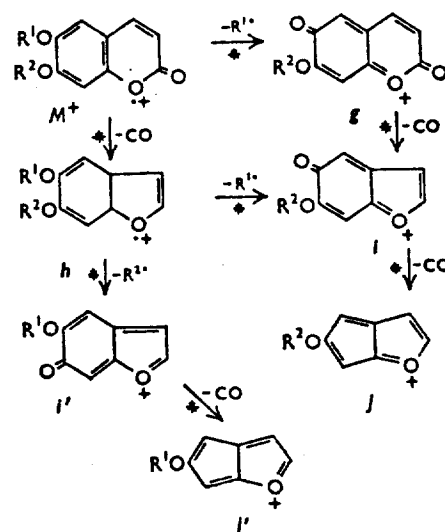
Scheme 2

* Metastable peak observed

chromone ring dominate the spectra of (I) and (IV) and can be rationalised as shown in Scheme 1 for (I).*

* The compositions of the molecular ion and major fragments were determined by high resolution measurements.

¹² C. S. Barnes, J. L. Occolowitz, *Austral. J. Chem.*, 1964, **17**, 975; N. S. Wulfson, V. I. Zaretskii, and V. G. Zyakoou, *Izvest. Akad. Nauk S.S.S.R., Ser. khim.*, 1963, 2215; R. A. W. Johnstone, B. J. Millard, F. M. Dean, and A. W. Hill, *J. Chem. Soc. (C)*, 1966, 1712.



Scheme 3

* Metastable peak observed

¹³ B. Willhalm, A. F. Thomas, and F. Gautschi, *Tetrahedron*, 1964, **20**, 1185.

The spectrum of xanthyletin (V) is, as expected for a dimethylchromene,¹³ very simple. The pyrylium ion (a, m/e 213; Scheme 2) carries 55% of the total ion current.

The fragmentation of scopoletin (VI) and its isomer (VII) can be summarised in terms of the fragmentation of (VIII) established by Djerassi and Shapiro⁹ (Scheme 3). The intensities of the major fragments are shown in Table 2. The relative intensities of the $M - 15$ peaks provide a ready means of demonstrating the presence of a 6-methoxy-substituent in simple coumarins.

EXPERIMENTAL

Mass spectra were obtained with an A.E.I. MS9 high resolution mass spectrometer using direct sample insertion. High resolution measurements were carried out using perfluorotributylamine as an internal standard, at a resolution of 15,000 (5% valley definition). Nuclear magnetic resonance spectra were obtained with a Perkin-Elmer R10 spectrometer for $CDCl_3$ solutions. Thin-layer chromatography analyses were carried out on Kieselgel HF plates developed with ether.

Isolation.—The fresh seeds, leaves, and stems (1.45 kg.) of *Anethum graveolens* were macerated in a Waring blender with chloroform. The dried extract was evaporated and the ether-soluble material was chromatographed on silica gel using gradient elution [3% ether in light petroleum (b. p. 30–40°) (1 l.) enriched with ether (1 l.); 50 c.c. fractions collected].

(a) 6,7-Dihydro-8,8-dimethyl-2H,8H-benzo[1,2-b:5,4-b']-dipyran-2,6-dione (I).—Those fractions (5–14) exhibiting λ_{max} 3430, 3310, 3070, 2980, and 2545 Å, were combined and evaporated and the residual pale green oil purified by repeated preparative t.l.c. [1 mm Kieselgel HF plates developed with ether]. Extraction of the band exhibiting a blue fluorescence when viewed under u.v. light yielded the pyranocoumarin (I) which crystallised from methanol as white rectangular plates (120 mg.), m. p. 177.5–178° (Found: C, 69.1; H, 4.9. $C_{14}H_{12}O_4$ requires C, 68.8; H, 4.9(5%). λ_{max} (in ethanol) 3425, 3300, 3070, 2980, 2545, 2280, and 2225 Å (ϵ 12,200, 10,800, 11,600, 11,000, 28,500, 13,600, and 14,300); ν_{max} (in CS_2): 1751 (α,β -unsaturated S-lactone); 1698 (aryl ketone); 1297, 822 (conjugated

cis-CH=CH), 1143 cm^{-1} (C–O–C); n.m.r. (Table 1) and mass spectrum (Figure 2).

6,7-Dihydroxy-6-hydroxy-8,8-dimethyl-2H,8H-benzo-[1,2-b:5,4-b']dipyran-2-one (IV).—Potassium borohydride (43 mg.) in water (1 c.c.) was added dropwise to an ice cooled, vigorously stirred solution of the aforementioned diketone (54 mg.) in methanol (20 c.c.). After 30 min., water was added and the whole extracted with chloroform and dried. Evaporation of the solvent afforded (IV) which crystallised from benzene as clusters of irregular plates, m. p. 167–168° (Found: C, 68.3; H, 5.7. $C_{14}H_{14}O_4$ requires C, 68.3; H, 5.7%). λ_{max} (in ethanol) 3300, 2590, 2485, and 2215 Å (ϵ 16,600, 3100, 3400, and 13,900); ν_{max} (KBr disc): 3470 (OH), 1702 (α,β -unsaturated S-lactone); 1630, 1291, 820 (conjugated *cis*-CH=CH); 1608, 1561, 1495 (aromatic C=C); 1145 cm^{-1} (C–O–C); n.m.r. (Table 1) and mass spectrum (Figure 3).

Xanthyletin (V).—The foregoing alcohol (25 mg.) and toluene-*p*-sulphonic acid (2 mg.) were heated under reflux in dry benzene (5 c.c.) for 5 min. Removal of the solvent under reduced pressure and purification of the residual oil by t.l.c. [0.5 mm Kieselgel HF plates developed with ether] yielded xanthyletin (V) which crystallised from methanol as irregular white plates, m. p. and mixed m. p. with an authentic specimen 126–127° (lit.,⁷ m. p. 128–127°); n.m.r. (Table 1) and mass spectrum (Scheme 2).

(b) **Scopoletin (VI).** The final fractions from the chromatography of the crude plant extract described earlier were found to contain scopoletin (IV) which, after purification by t.l.c. (Kieselgel HF plates developed with chloroform), crystallised from methanol as pale yellow needles (3 mg.), m. p. 203–204° (lit.,⁸ m. p. 204°); n.m.r. (Table 1) and mass spectrum (Table 2).

Methylation of scopoletin with diazomethane gave 6,7-dimethoxycoumarin (VIII), which crystallised from water as fine white needles, m. p. 142–143° (lit.,³ m. p. 144°), undepressed on admixture with an authentic sample obtained by the hydrolysis and subsequent methylation of aesculin.

The authors gratefully acknowledge the receipt of an Imperial Chemical Industries postdoctoral fellowship (to C. B. P.) and thank Dr. J. W. W. Morgan for the sample of xanthyletin.

[7/770 Received, June 6th, 1967]

The spectrum of xanthyletin (V) is, as expected for a dimethylchromene,¹³ very simple. The pyrylium ion (a , m/e 213; Scheme 2) carries 55% of the total ion current.

The fragmentation of scopoletin (VI) and its isomer (VII) can be summarised in terms of the fragmentation of (VIII) established by Djerassi and Shapiro⁹ (Scheme 3). The intensities of the major fragments are shown in Table 2. The relative intensities of the $M - 15$ peaks provide a ready means of demonstrating the presence of a 6-methoxy-substituent in simple coumarins.

EXPERIMENTAL

Mass spectra were obtained with an A.E.I. MS9 high resolution mass spectrometer using direct sample insertion. High resolution measurements were carried out using perfluorotributylamine as an internal standard, at a resolution of 15,000 (5% valley definition). Nuclear magnetic resonance spectra were obtained with a Perkin-Elmer R10 spectrometer for $CDCl_3$ solutions. Thin-layer chromatography analyses were carried out on Kieselgel HF plates developed with ether.

Isolation.—The fresh seeds, leaves, and stems (1.45 kg.) of *Anethum graveolens* were macerated in a Waring blender with chloroform. The dried extract was evaporated and the ether-soluble material was chromatographed on silica gel using gradient elution (3% ether in light petroleum (b. p. 30–40°) (1 l.) enriched with ether (1 l.); 50 c.c. fractions collected).

(a) 6,7-Dihydro-8,8-dimethyl-2H,8H-benzo[1,2-b:5,4-b']-dipyran-2,6-dione (I).—Those fractions (5–14) exhibiting λ_{max} 3430, 3310, 3070, 2980, and 2545 Å, were combined and evaporated and the residual pale green oil purified by repeated preparative t.l.c. [1 mm Kieselgel HF plates developed with ether]. Extraction of the band exhibiting a blue fluorescence when viewed under u.v. light yielded the pyranocoumarin (I) which crystallised from methanol as white rectangular plates (120 mg.), m. p. 177.5–178° (Found: C, 69.1; H, 4.9. $C_{14}H_{12}O_4$ requires C, 68.8; H, 4.9(5%)). λ_{max} (in ethanol) 3425, 3300, 3070, 2980, 2545, 2280, and 2225 Å (ϵ 12,200, 10,800, 11,600, 11,000, 28,500, 13,600, and 14,300); ν_{max} (in CS_2): 1751 (α,β -unsaturated S-lactone); 1698 (aryl ketone); 1297, 822 (conjugated

cis-CH=CH), 1143 cm^{-1} (C–O–C); n.m.r. (Table 1) and mass spectrum (Figure 2).

6,7-Dihydroxy-6-hydroxy-8,8-dimethyl-2H,8H-benzo[1,2-b:5,4-b']dipyran-2-one (IV).—Potassium borohydride (45 mg.) in water (1 c.c.) was added dropwise to an ice cooled, vigorously stirred solution of the aforementioned diketone (54 mg.) in methanol (20 c.c.). After 30 min., water was added and the whole extracted with chloroform and dried. Evaporation of the solvent afforded (IV) which crystallised from benzene as clusters of irregular plates, m. p. 167–168° (Found: C, 68.3; H, 5.7. $C_{14}H_{14}O_4$ requires C, 68.3; H, 5.7%). λ_{max} (in ethanol) 3300, 2590, 2485, and 2215 Å (ϵ 16,600, 3100, 3400, and 13,900); ν_{max} (KBr disc): 3470 (OH), 1702 (α,β -unsaturated S-lactone); 1630, 1291, 820 (conjugated *cis*-CH=CH); 1608, 1561, 1495 (aromatic C=C); 1145 cm^{-1} (C–O–C); n.m.r. (Table 1) and mass spectrum (Figure 3).

Xanthyletin (V).—The foregoing alcohol (25 mg.) and toluene-*p*-sulphonic acid (2 mg.) were heated under reflux in dry benzene (5 c.c.) for 5 min. Removal of the solvent under reduced pressure and purification of the residual oil by t.l.c. [0.5 mm. Kieselgel HF plates developed with ether] yielded xanthyletin (V) which crystallised from methanol as irregular white plates, m. p. and mixed m. p. with an authentic specimen 126–127° (lit.,⁷ m. p. 126–127°); n.m.r. (Table 1) and mass spectrum (Scheme 2).

(b) **Scopoletin (VI).** The final fractions from the chromatography of the crude plant extract described earlier were found to contain scopoletin (IV) which, after purification by t.l.c. (Kieselgel HF plates developed with chloroform), crystallised from methanol as pale yellow needles (3 mg.), m. p. 203–204° (lit.,⁸ m. p. 204°); n.m.r. (Table 1) and mass spectrum (Table 2).

Methylation of scopoletin with diazomethane gave 6,7-dimethoxycoumarin (VIII), which crystallised from water as fine white needles, m. p. 142–143° (lit.,³ m. p. 144°), undepressed on admixture with an authentic sample obtained by the hydrolysis and subsequent methylation of aesculin.

The authors gratefully acknowledge the receipt of an Imperial Chemical Industries postdoctoral fellowship (to C. B. P.) and thank Dr. J. W. W. Morgan for the sample of xanthyletin.

[1/770 Received, June 6th, 1967]

cated administration of Diodoquin followed by carbarsone. Simultaneous use of succinylsulfathiazole and Diodoquin was found to be effective by El-Ghaffar (*J. Roy. Egyptian M. A.*, 1949, 32, 24). In amebic abscess of the liver, Zavala and Hamilton (*Ann. Int. Med.*, 1952, 36, 110) obtained the best results with Diodoquin and chloroquine. Liver function tests show no evidence of liver damage during treatment with Diodoquin or carbarsone. Use of tetracycline antibiotics is discouraged because of the disturbance of intestinal flora they produce (Knight and Tarun, *Am. J. Trop. Med.*, 1952, 32, 727).

OTHER USES.—Diodoquin has been found to be effective in balantidiasis (Shookhoff, *ibid.*, 1951, 31, 442). In *Trichomonas vaginalis* vaginitis cure in 88 per cent of patients treated resulted from use of cleansing acid douches followed by insertion of 1 or 2 vaginal tablets containing 100 mg. of Diodoquin every 12 hours for 12 days although to prevent relapse treatment may be continued for 4 to 8 weeks.

Toxicology.—Severe dermatitis following use of diiodohydroxyquin has been reported (David, *J.A.M.A.*, 1945, 129, 572; see also Leifer and Steiner, *J. Invest. Dermat.*, 1951, 17, 233). Development of furunculosis in two patients, and of chills, fever, rash and erythema in a third, have also been described (Silverman and Leslie, *J.A.M.A.*, 1945, 128, 1080).

Dose.—The usual dose is 650 mg. (about 10 grains), by mouth, 3 times daily for 20 days; the range of dose is 650 mg. to 1 Gm. For children the dose is 200 mg. for each 7 Kg. (approximately 15 pounds) of body weight, within the dosage limits just stated, 3 times daily for 20 days. A vaginal tablet (*Floraquin*, Searle), containing 100 mg. of diiodohydroxyquin, with lactose, dextrose and boric acid to promote an acid reaction in the vagina is used once or twice daily.

Storage.—Preserve "in well-closed containers." *U.S.P.*

DIIDOHYDROXYQUIN TABLETS. *U.S.P.*

"Diiodohydroxyquin Tablets contain not less than 93 per cent and not more than 107 per cent of the labeled amount of $C_9H_5I_2NO$." *U.S.P.*

Usual Sizes.—200 and 650 mg. (approximately 3 and 10 grains).

DILL OIL. *B.P.* *Oleum Anethi*

Dill Oil is the volatile oil distilled from the dried ripe fruits of *Anethum graveolens* L. It contains not less 43.0 per cent w/w and not more than 63.0 per cent w/w of carvone, $C_{10}H_{14}O$.

Fr. Essence d'aneth. Ger. Dillöl.

Dill oil is colorless or of a pale yellow color, with the odor of the fruit, and has a hot, sweetish, acid taste. Its weight per ml., at 20°, is between 0.895 and 0.910 Gm. The optical rotation is from +70° to +80°; the refractive index is from 1.481 to 1.492.

The assay for carvone is the same as for car-

vone in caraway oil (*B.P. method*), which utilizes the reaction with hydroxylamine hydrochloride, followed by titration of liberated acid with 1 N potassium hydroxide.

Dill oil contains from 40 to 65 per cent of carvone, considerable *d*-limonene and smaller amounts of other terpenes; English and Spanish oils also contain phellandrene which, it is said, does not occur in oil of German origin.

East Indian dill oil, which is occasionally used as an adulterant or substitute, comes from a different plant (*Anethum Sowa* Roxb.). It differs from the genuine in containing less carvone; a small amount of crystalline residue is also present which is stated to consist of paraffin. Oil of dill should be kept in a well-closed container, protected from light and stored in a cool place.

Dill oil is used as an aromatic carminative, particularly in the form of either concentrated dill water or dill water. The dose of dill oil is given by the *B.P.* as 0.06 to 0.2 ml. (approximately 1 to 3 minims).

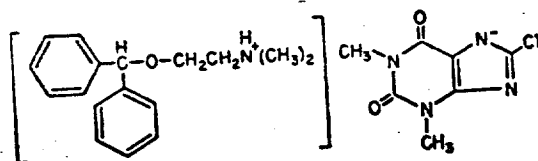
CONCENTRATED DILL WATER. *B.P.*

Concentrated Dill Water is made by dissolving 20 ml. of dill oil in 600 ml. of 90 per cent alcohol, with enough distilled water to make 1000 ml. Powdered talc is added as a filtering medium; the preparation is occasionally shaken for a few hours and then filtered. It contains approximately 54 per cent of alcohol.

Although concentrated dill water may be used undiluted, as an aromatic carminative, it is generally employed diluted with 39 volumes of distilled water to provide essentially the equivalent of dill water prepared by saturating distilled water with the oil; such a diluted water contains about 1.3 per cent alcohol.

The *B.P. dose* of concentrated dill water is 0.3 to 1 ml. (approximately 5 to 15 minims); the dose of the diluted water is 15 to 30 ml. (approximately ½ to 1 fluidounce).

DIMENHYDRINATE. *U.S.P.*



"Dimenhydrinate contains not less than 53 per cent and not more than 55.5 per cent of diphenhydramine ($C_{17}H_{21}NO$), and not less than 44 per cent and not more than 47 per cent of 8-chlorotheophylline ($C_7H_7ClN_4O_2$)." *U.S.P.*

Dramamine (Searle).

This salt is the product of the interaction of the antihistaminic base diphenhydramine with the acidic compound 8-chlorotheophylline. For details of synthesis see U. S. Patent 2,499,053 (1950).

Description.—Dimenhydrinate occurs as a white, crystalline, odorless powder. Dimenhydrinate is slightly soluble in water. It is freely solu-

OIL DILLWEED, AMERICAN

SCIENTIFIC SECTION
ESSENTIAL OIL ASSOCIATION OF U. S. A.

2 Lexington Avenue, New York 10, N. Y.

E.O.A. STANDARD for: OIL DILLWEED, AMERICAN

Oil Dillweed is distilled from the plant, which includes the stalks, leaves and seeds. It should not be confused with the oil from the seeds alone. The principal producing areas are in the States of Oregon and Indiana, some oil is produced in Idaho, Michigan and Ohio. Distillation takes place in the late summer and

early fall. The bulk of the oil is used in the pickle and canning industry. Some Oil Dillweed is produced in Europe but does not usually conform to the specifications for American oil due to its lower carvone content.

SPECIFICATIONS

Other General Names	Oil Dill Oil Dill Herb
Botanical Nomenclature	Anethum Graveolens, L Peucedanum Graveoleas, Bentham.
Preparation	Obtained by steam distillation of the freshly cut plants.
Physical & Chemical Constants	Color & Appearance: Light yellow to yellow liquid. Specific Gravity @ 25/25°C: 0.884 to 0.0900. (Temp. Correction factor from n°/n°C: 0.00053 per °C.) Optical Rotation: +8½° to +95°. Refractive Index @ 20°C: 1.4800 to 1.4850. Solubility in Alcohol: Soluble in 1 volume and more of 90% alcohol. Carvone Content: 28% to 45% (See Note 1*).
Descriptive Characteristics	Proceed as directed for the determination of Aldehydes and Ketones by the Neutral Sulphite method (See Determinations EOA No. 1-J).
	Stability: Acids: Stable in the presence of weak organic acids. Alkali: Relatively stable to weak alkalis.
	Solubility: Benzyl Benzoate: Soluble in all proportions. Fixed Oils: Soluble in all proportions in most fixed oils. Glycerine: Practically insoluble. Mineral Oil: Soluble in all proportions. Propylene Glycol: Usually soluble with opalescence or turbidity.
Containers	Should be shipped preferably in glass, tin-lined or aluminum containers. Good quality galvanized containers are suitable when long storage is not contemplated.
Storage	Store preferably in tight, full containers in a cool place protected from light.
Notes	*Note 1: Some oil may show a minimum carvone content of 25% with a corresponding lower specific gravity, lower refractive index and higher optical rotation. This type oil is usually obtained from early season distillations of the herb.

OIL DILL SEED EUROPEAN

SCIENTIFIC SECTION

ESSENTIAL OIL ASSOCIATION OF U. S. A.

2 Lexington Ave., New York 10, N.Y.

E.O.A. STANDARD for: OIL DILL SEED EUROPEAN

Dill Seed oil is the volatile oil obtained by steam distillation of the fruit (or seeds) of *Anethum graveolens*, L.

This monograph covers the oil obtained from the seed cultivated and grown in various European coun-

tries. It differs considerably from the Indian Dill Seed Oil in odor and flavor.

The flavor of Dill Seed Oil European, due to its high carvone content, resembles that of Caraway Seed Oil.

SPECIFICATIONS

Botanical Nomenclature

Anethum graveolens, L.
(Family: *Umbelliferae*.)

Preparation

Obtained by steam distillation of the crushed dried fruit.

Physical and Chemical Constants

Appearance and Odor: Slightly yellowish to light yellow liquid with a caraway-like odor and flavor.

Specific Gravity at 25°/25°C: 0.890 to 0.915.
(Temperature correction factor from n°/n°C: 0.00056 per °C.)

Optical Rotation: +70° to +82°.

Refractive Index at 20°C: 1.4330 to 1.4900.

Carvone Content: 42% to 60%.

Assay: Proceed as directed for the determination of aldehydes and ketones by the neutral sulphite method (See Determinations EOA No. 1-J.)

Solubility in Alcohol: Soluble in 2 and more volumes of 80% alcohol occasionally with slight opalescence.

Descriptive Characteristics

Solubility:

Benzyl Benzoate: Soluble in all proportions.

Diethyl Phthalate: Soluble in all proportions.

Fixed Oils: Soluble in all proportions in most fixed oils.

Glycerine: Practically insoluble.

Mineral Oil: Soluble in all proportions.

Propylene Glycol: Soluble with slight opalescence.

Stability:

Acids: Relatively stable to weak acids.

Alkali: Relatively stable to weak alkali.

Containers

Ship preferably in glass, aluminum or other suitably lined containers. Good quality galvanized containers are suitable when long storage is not contemplated.

Storage

Store in tight, full containers in a cool place protected from light.

SCIENTIFIC SECTION

ESSENTIAL OIL ASSOCIATION OF U. S. A.

2 Lexington Ave., New York 10, N.Y.

E.O.A. STANDARD for: OIL DILL SEED INDIAN

The essential oil distilled from the Indian dill seed differs in its physical properties, odor and flavor, from the European and American varieties. The prin-

cipal reason for this difference, is the presence of dillapiole. Commercially it is less important than the American dill weed oil.

SPECIFICATIONS

Other General Names	Oil Dill Indian. Oil Dill Seed East Indian.
Botanical Nomenclature	<i>Anethum Sowa</i> D.C. (A. sowa, Noxb.) (Family: <i>Umbelliferae</i> .)
Preparation	Obtained by steam distillation of the crushed mature fruit.
Physical and Chemical Properties	Appearance and Odor: Light yellow to light brown with a rather harsh caraway like odor and flavor. Specific Gravity at 25°C/25°C: 0.925 to 0.980. (Temperature correction factor from n°/n°C = 0.00070 per °C.) Optical Rotation: +40° to +58°. Refractive Index at 20°C: 1.4860 to 1.4950. Carvone Content: 20% to 30%. Assay: Proceed as directed for the determination of aldehydes and ketones by the neutral sulphite method. (See Determinations EOA #1-J) Prolonged heating and agitation may be necessary for the complete reaction. Keep flask stoppered to prevent loss. Solubility in Alcohol: Soluble in 0.5 and more volumes of 90% alcohol. Occasionally oils with high carvone content are soluble in 3 to 10 volumes of 80% alcohol.
Descriptive Characteristics	Solubility: Benzyl Benzoate: Soluble in all proportions. Diethyl Phthalate: Soluble in all proportions. Fixed Oils: Soluble in all proportions in most fixed oils. Glycerine: Relatively insoluble. Mineral Oil: Soluble in all proportions with occasional slight opalescence. Propylene Glycol: Relatively soluble. Stability: Acids: Stable to weak organic acids. Alkali: Relatively stable to weak alkali.
Containers	Ship preferably in glass, aluminum or other suitably lined containers.
Storage	Store preferably in tight, full containers protected from light.

Packaging and storage. Store in full, tight, preferably glass, aluminum, or other suitably lined containers in a cool place protected from light.

Functional use in foods. Flavoring agent.

DILL SEED OIL, INDIAN

Dill Seed Oil, East Indian; Dill Oil, Indian

DESCRIPTION

The volatile oil obtained by steam distillation from the crushed mature fruit of Indian dill, *Anethum sowa* D.C. (Fam. *Umbelliferae*). It is a light yellow to light brown liquid with a rather harsh caraway-like odor and flavor. It is soluble in most fixed oils and in mineral oil, occasionally with slight opalescence. It is sparingly soluble in propylene glycol and practically insoluble in glycerin.

SPECIFICATIONS

Assay. Not less than 20 per cent and not more than 30 per cent, by volume, of ketones as carvone ($C_{10}H_{14}O$).

Angular rotation. Between $+40^\circ$ and $+58^\circ$.

Refractive index. Between 1.4860 and 1.4950 at 20° .

Solubility in alcohol. Passes test.

Specific gravity. Between 0.925 and 0.980.

Limits of Impurities

Arsenic (as As). Not more than 3 parts per million (0.0003 per cent)

Heavy metals (as Pb). Not more than 40 parts per million (0.004 per cent).

Lead. Not more than 10 parts per million (0.001 per cent).

TESTS

Assay. Proceed as directed under *Aldehydes and Ketones—Neutral Sulfite Method*, page 742.

Angular rotation. Determine in a 100-mm. tube as directed under *Optical Rotation*, page 780.

Refractive index, page 785. Determine with an Abbé or other refractometer of equal or greater accuracy.

Solubility in alcohol. Proceed as directed in the general method, page 746. One ml. dissolves in 0.5 ml. of 90 per cent alcohol and remains clear on dilution.

Specific gravity. Determine by any reliable method (see page 4).

Arsenic. A *Sample Solution* prepared as directed for organic compounds meets the requirements of the *Arsenic Test*, page 720.

Heavy metals. Prepare and test a 500-mg. sample as directed in *Method II* under the *Heavy Metals Test*, page 763, using 20 mcg. of lead ion (Pb) in the control (*Solution A*).

Lead. A *Sample Solution* prepared as directed for organic compounds meets the requirements of the *Lead Limit Test*, page 772, using 10 mcg. of lead ion (Pb) in the control.

Packaging and storage. Store in full, tight, preferably glass, aluminum, or other suitably lined containers protected from light.

Functional use in foods. Flavoring agent.

DILLWEED OIL, AMERICAN

Dill Oil; Dill Herb Oil

DESCRIPTION

The volatile oil obtained by steam distillation from the freshly cut stalks, leaves and seeds of the plants, *Anethum graveolens*, L. It is a light yellow to yellow liquid. It is soluble in most fixed oils and in mineral oil. It is soluble, usually with opalescence or turbidity, in propylene glycol, but it is practically insoluble in glycerin.

SPECIFICATIONS

Assay. Usually not less than 28 per cent and not more than 45 per cent, by volume, of ketones as carvone ($C_{10}H_{14}O$).

Note: Oil obtained from early season distillation may show a carvone content as low as 25 per cent and a correspondingly lower specific gravity, lower refractive index, and a higher angular rotation.

Angular rotation. Between $+84^{\circ}$ and $+95^{\circ}$.

Refractive index. Between 1.4800 and 1.4850 at 20° .

Solubility in alcohol. Passes test.

Specific gravity. Between 0.884 and 0.900.

Limits of Impurities

Arsenic (as As). Not more than 3 parts per million (0.0003 per cent).

Heavy metals (as Pb). Not more than 40 parts per million (0.004 per cent).

Lead. Not more than 10 parts per million (0.001 per cent).

TESTS

Assay. Proceed as directed under *Aldehydes and Ketones—Neutral Sulfite Method*, page 742.

Angular rotation. Determine in a 100-mm. tube as directed under *Optical Rotation*, page 780.

Refractive index, page 785. Determine with an Abbé or other refractometer of equal or greater accuracy.

Solubility in alcohol. Proceed as directed in the general method, page 746. One ml. dissolves in 1 ml. of 90 per cent alcohol, frequently with opalescence which may not disappear on dilution to as much as 10 ml.

Specific gravity. Determine by any reliable method (see page 4).

Arsenic. A *Sample Solution* prepared as directed for organic compounds meets the requirements of the *Arsenic Test*, page 720.

Heavy metals. Prepare and test a 500-mg. sample as directed in *Method II* under the *Heavy Metals Test*, page 763, using 20 mcg. of lead ion (Pb) in the control (*Solution A*).

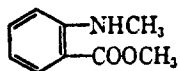
Lead. A *Sample Solution* prepared as directed for organic compounds meets the requirements of the *Lead Limit Test*, page 772, using 10 mcg. of lead ion (Pb) in the control.

Packaging and storage. Store in full, tight, preferably glass, aluminum, or tin-lined containers in a cool place protected from light.

Functional use in foods. Flavoring agent.

DIMETHYL ANTHRANILATE

Methyl *N*-Methyl Anthranilate



$\text{C}_9\text{H}_{11}\text{NO}_2$

Mol. wt. 161.19

DESCRIPTION

A pale yellow liquid having a bluish fluorescence and a grape-like odor. It may contain small amounts of methyl anthranilate which is limited by the upper assay tolerance and by the solidification point. It is practically insoluble in water and in glycerin, partially soluble in propylene glycol, and soluble in most fixed oils.

SPECIFICATIONS

Assay. Not less than 98 per cent and not more than the equivalent of 101.3 per cent of $\text{C}_9\text{H}_{11}\text{NO}_2$.

sol in an equal vol of alcohol and of glacial acetic acid. *Keep well closed, cool, and protected from light.*

USE: As flavor in foods and in perfumes.

MED USE: Carminative.

Oil of Cinnamon, Ceylon. Volatile oil from bark of Ceylon cinnamon. *Constit.* 50-65% cinnamaldehyde; 4-8% eugenol; phellandrene.

Light yellow liq; gradually becomes reddish; characteristic odor. d_{4}^{20} 1.000-1.030. Rotation 0° to -2° in a 100-mm tube. n_D^{20} 1.565-1.582.

MED USE: See Oil of Cinnamon.

Oil of Citronella. Volatile oil from fresh grass of *Cymbopogon (Andropogon) nardus* (L.) Rendle, *Gramineae*. *Constit.* Ceylon: about 60% geraniol, about 15% citronellol, 10-15% camphene and dipentene, small quantities of linalool, borneol. Java: 85-90% of geraniol.

Almost colorless to pale yellow liq; gradually becomes reddish; pleasant odor. d_{4}^{20} Ceylon, 0.897-0.912; Java, 0.885-0.900. Rotation: Ceylon, -6° to -14°; Java, -2° to -5° in a 100-mm tube at 20°. n_D^{20} Ceylon 1.479-1.485; Java, 1.468-1.473. Slightly sol in water; sol in 10 vols 80% alcohol. *Keep well closed, cool, and protected from light.*

USE: As perfume; insectifuge.

Oil of Clove. Clove oil. Volatile oil from dried flower buds of *Eugenia caryophyllata* Thunb. (*Caryophyllus aromaticus* L.), *Myrtaceae*. *Constit.* 82-87% eugenol, including about 10% acetylene; caryophyllene, small quantities of furfural, vanillin, methyl amyl ketone.

Colorless to pale yellow liq, becoming darker and thicker with age. d_{4}^{25} 1.038-1.050. Rotation not over -1°10' in 100-mm tube at 25°. n_D^{25} 1.530. bp about 250°. Insoluble in water; sol in 2 vols 70% alcohol; very sol in stronger alcohol, in ether, glacial acetic acid. *Keep well closed, cool, and protected from light.*

USE: In confectionery, toothpowders; also in microscopy.

MED USE: Local anesthetic in toothache; counterirritant; has been used as carminative.

Oil of Copaiba. Volatile oil from copaiba balsam, usually Maracaibo. *Constit.* Caryophyllene—the chief and only well-defined constituent.

Colorless or pale yellow liquid. d_{4}^{25} 0.895-0.905, increasing with age. bp 250-275°. Rotation -7° to -35° in 100-mm tube. n_D^{25} 1.495-1.500. Insoluble in water; very sol in alcohol, ether, carbon disulfide. *Keep well closed, cool, and protected from light.*

Oil of C
Coriandrum
coriandrol;
hyde.

Colorless;
+8° to +11°
Almost insol
stronger alco
acid. *Keep w*

USE: Flavo
MED USE: I

Oil of Cnb
L.f., *Piperac*
camphor—the

Colorless, r

Rotation -20

1.5020. Insol

miscible with
cool, and prote

MED USE: Fc

Oil of Cumin. Volatile oil from fruit *Cuminum cyminum* L., *Umbelliferae*. *Constit.* 30-40% cuminaldehyde; β -cymene, β -pinene, dipentene.

Colorless to yellow liquid. d_{4}^{25} 0.900-0.935. Rotation +4° to +8° in a 100-mm tube at 20°. n_D^{20} 1.4950-1.5090. Almost insol in water; sol in 10 vols 80% alcohol; more sol in stronger alcohol; very sol in chloroform, ether. *Keep well closed, cool, and protected from light.*

Oil of Cypress. Volatile oil from leaves and young branches of *Cupressus sempervirens* L., *Pinaceae*. *Constit.* Furfural, α -pinene, β -camphene, cymene, β -terpineol, β -cadinene, sylvestrene, cypress camphor.

Yellowish liquid. d_{4}^{20} 0.88-0.89. Rotation +4° to +18° in a 100-mm tube at 20°. Slightly sol in water; sol in 2-6 vols 90% alcohol. *Keep well closed, cool, and protected from light.*

Oil of Dill. Volatile oil from dried ripe fruit of *Anethum graveolens* L., *Umbelliferae*. *Constit.* About 50% carvone β -limonene, phellandrene and other terpenes.

Colorless or pale yellow liq; characteristic odor. d_{4}^{25} 0.900-0.915. Rotation +70° to +80° in 100-mm tube at 20°. n_D^{20} 1.481-1.492. Insoluble in water; sol in 1 vol 90% alcohol.

Keep well closed, cool, and protected from light.

MED USE: Aromatic carminative.

Oil of Dwarf Pine Needles. Oil of mountain pine; oil *Pinus pumilio*. Volatile oil from fresh leaves of *Pinus montana* Mill. (*P. pumilio* Haecke), *Pinaceae*. *Constit.* β -Pinene, β -phellandrene, sylvestrene, dipentene, β -cadinene, 5-7% bornyl acetate.

Colorless or faintly yellow liq; pleasant odor; bitter taste. d_{4}^{25} 0.853-0.869. Rotation -5° to -12° in 100-mm tube at 25°. n_D^{25} 1.4750-1.4800. Insoluble in water; sol in 4.5-8 vols 90% alcohol; very sol in chloroform, ether. *Keep well closed, cool, and protected from light.*

MED USE: Has been used as expectorant, inhalant, anti-rheumatic.

Oil of Eucalyptus. Dinkum oil. Volatile oil from fresh leaves of *Eucalyptus globulus* Labill and of some other species of *Eucalyptus*, *Myrtaceae*. A dwarf species, called Mallee in Australia, is richest in oil of Eucalyptus.

Constit. 70-80% cineole (eucalyptol); α -pinene; phellandrene; terpineol; citronellal; geranyl acetate; eudesmol; eudesmyl acetate; piperitone; volatile aldehydes (principally isovaleric); E. Guenther, *The Essential Oils* vol. 4 (van Nostrand, New York, 1950), pp 437-525.

Colorless to pale yellow liq; characteristic camphoraceous odor; pungent, spicy, cooling taste. d_{4}^{25} 0.905-0.925. Solidif not below -15.4°. Rotation -5° to +5° in 100-mm tube. n_D^{25} 1.4580-1.4700. Almost insol in water; sol in 5 vols 70% alcohol; miscible with abs alcohol, oils, fats. *Keep well closed, cool, and protected from light.*

MED USE: Expectorant, vermifuge, local antiseptic.

VET USE: In bronchitis as an inhalant and by mouth as a stimulant. *As and cattle: 8-15 ml;*

*of dried fruit of Foenicu-
tit.* 50-60% anethole,
ie, dipentene, phellan-

r and taste of fennel.
24° in 100-mm tube at
in water; sol in 1 vol
1 in chloroform, ether.
om light.
edifices.

fr. Volatile oil from
Mill. (*A. picea* Lindl.,
 β -Pinene, β -limonene,

terebinthinate taste.
9° in a 100-mm tube
ols 90% alcohol, in
and protected from light.

MED USE: See Oil of Dwarf Pine Needles.

Oil of Fir—Siberian. Oil of pine; oleum abietis. Volatile oil from fresh leaves of *Abies sibirica* Ledeb., *Pinaceae*. *Constit.* About 40% esters calculated as bornyl acetate; β -pinene camphene, dipentene, and phellandrene.

Colorless or pale yellow liq; aromatic odor; pungent taste. d_{4}^{25} 0.905-0.925. Rotation -32° to -45° in 100-mm tube at 20°. n_D^{20} 1.456-1.476. Soluble in an equal vol 90% alcohol. *Keep well closed, cool, and protected from light.*

MED USE: See Oil of Dwarf Pine Needles.

Merck Index

8th Ed. 1968

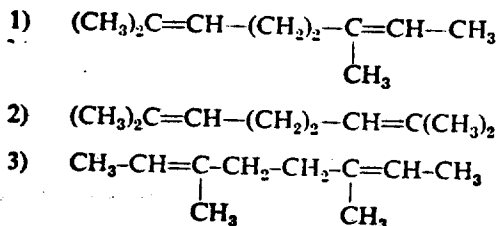
40a

Perfume and Flavor Chemicals 1956. Arctander, S.

974: DI ISOPRENE

The commercial product is normally a mixture of:

- 1) 2,6-Dimethyl-2,6-octadiene.
- 2) 2,7-Dimethyl-2,6-octadiene.
- 3) 3,6-Dimethyl-2,6-octadiene.



$$\text{C}_{10}\text{H}_{18} = 138.25$$

Colorless, mobile liquid. Insoluble in water, soluble in alcohol and oils.

Sweet, diffusive, somewhat "gassy" odor.

Has been suggested for use in masking odors for industrial purposes. Could possibly find small use in Styrax compositions, etc.

Overall of very little interest to the perfumer.

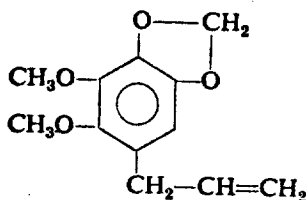
Prod.: by dimerization of Isoprene, using Hydrogen for hydrogen addition in presence of Potassium and Ethyl alcohol.

67-399;

975: DILL APIOLE

1,2-Methylene dioxy-4-allyl-5,6-dimethoxybenzene.

An isomer of Parsley-apiole.



$$\text{C}_{12}\text{H}_{14}\text{O}_4 = 222.24$$

Viscous, almost colorless liquid. B.P. 285° C.

Practically insoluble in water, soluble in alcohol and oils, almost insoluble in Propylene glycol.

Very faint, warm-woody odor. The effect is, however, quite perceptible when this material is used in combination with lower boiling fragrance materials.

Very rarely used in perfumes.

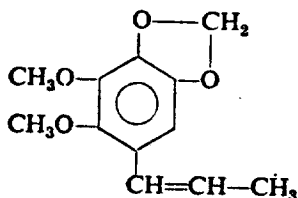
Probably not used in flavors.

Prod.: from East Indian Dill seed oil by isolation. Or: synthetically from Gallacetophenone dimethylether.

65-539; 72-92; 90-487;

976: DILL-iso-APIOLE

1,2-Methylenedioxy-4-propenyl-5,6-dimethoxybenzene.



$$\text{C}_{12}\text{H}_{14}\text{O}_4 = 222.24$$

White or colorless crystals. M.P. 44° C. B.P. 296° C.

Insoluble in water, soluble in alcohol and oils.

Very faint, warm-camphoraceous and woody odor. When compared to Dill-apiole, it is more camphoraceous than that.

This chemical finds very little use in perfumery, perhaps no use at all in flavors, but it may be a component of certain artificial essential oils and herbal-spicy extracts.

Prod.: by isomerization of Dill apiole with alcoholic alkali.

72-93; 90-488;

Ind. Jour. Med. Res., 47, 5, September, 1959.

BIOFLAVONOIDS FROM INDIAN VEGETABLES AND FRUITS.

(Miss) K. GANJU, AND (Miss) B. PURI.

(From the Department of Nutrition, Lady Irwin College, New Delhi.)

[Received for publication, January 6, 1959.]

DURING the past quarter of a century interest has been shown on the marked physiological action of flavonoids. According to Seshadri (1948) the credit goes to Koike (1931) for the earliest report of the drug action of flavonoids following the latter's investigation of their diuretic action on normal rabbits. This work was supported by Fukuda (1932) who also claimed that these compounds were cardiac stimulants and vasoconstrictors, and that they increased blood pressure. Many of these flavonoids have also marked vitamin P action and the place of bioflavonoids in the treatment of various diseases has been recently established (Szent Gyorgyi, 1936, 1955-56). Claims have been made frequently that certain vegetables have medicinal properties and that they should be advocated for curing diseases (Gupta and Seshadri, 1952 ; Farooq *et al.*, 1953). Hence, in the present work, vegetables and fruits grown in India (Chatterjee and Randhawa, 1952) and which form a large portion of Indian dietary have been investigated for the availability of bioflavonoids.

MATERIALS AND METHODS.

1. *Chromatography*.—The alcoholic extracts from vegetables and fruits after preliminary purification and removal of chlorophyll by absorption on magnesol were examined by the method of filter-paper chromatography (horizontal migration) as described by Pankajamani and Seshadri (1952). However, the upper layer of phenol water was found to be a better general solvent for the large range of compounds consisting of chalcones, flavanones, flavones, flavonols and their glycosides. One per cent ammonia was used as spray and the temperature was 34°C. to 36°C. The bioflavonoids were characterized by comparison with R_f values of authentic samples run simultaneously and by their characteristic colour reactions as summarized below :—

Flavonones	: Almost colourless, pink colour with magnesium powder and hydrochloric acid and a yellow solution with sodium hydroxide.
Chalkones	: Yellow to red in colour, no colour with magnesium powder and hydrochloric acid but an orange-red colour with sodium hydroxide.
Flavones and flavonols	} Red colour with magnesium powder and hydrochloric acid, a yellow solution with sodium hydroxide and greenish yellow fluorescence with sulphuric acid.
3-Hydroxy flavanones	} Characteristic Pews reaction, i.e. pink colour with zinc and hydrochloric acid. This reaction is also positive for flavonol 3-glycosides.

2. *Isolation and estimation.*—Four-kilograms of fresh air-dried material in each case were extracted with cold rectified spirit three times, each extraction being continued for twenty four hours. The total extract was concentrated under reduced pressure and repeatedly shaken with petroleum ether till the chlorophyll was removed. The residue was dried in a vacuum desiccator, then taken in alcohol and repeatedly passed through a column of magnesol till almost a clear yellow solution was obtained. The entire yellow solution was further purified by treatment with neutral lead acetate when the quercetin glycoside was precipitated in the form of a bulky yellow lead salt. This was filtered off, suspended in alcohol and a current of hydrogen sulphide passed through it, till all the lead was removed in the form of lead sulphide. The black precipitate of lead sulphide was filtered off. The light yellow alcoholic solution containing the glycoside gave Pears test for flavanol-3-glycosides. It was hydrolysed using 7 per cent sulphuric acid and the product extracted with ether. The ether solution was concentrated and the residue dried and weighed. This weight was used for calculating the quercetin content. The product was twice crystallized from alcohol yielding tiny yellow crystals, m.p.; 316°C. to 317°C. It gave all the reactions of quercetin and the mixed m.p. with an authentic sample of quercetin was undepressed. The aqueous solution gave tests for reducing sugar.

3. In the materials which contained a good amount of flavonoids, the extraction, identification and estimation of vitamin K was also effected. For this purpose the air-dried foodstuffs were extracted with petroleum ether and the extract repeatedly passed through a column of magnesium oxide until all chlorophyll was removed and vitamin K was obtained as lemon yellow oil. It was then identified and estimated colorimetrically (Rangaswami and Seshadri, 1952).

RESULTS.

The results obtained by the circular-paper chromatography of the authentic samples of flavonoids are summarized in Table I.

A systematic study of large number of indigenous materials did not show the presence of bioflavonoids in the following vegetables and fruits :

Vegetables.—*Amorphophallus campanulatus* (telinga potato), *Cicer arietinum* (gram), *Brassica caulorapa* (knol khol), *Solanum tuberosum* (potato), *Calocasia esculenta* (arum), *Cucurbita moschata* (sweet gourd or pumpkin), *Brassica rapa* (turnip), *Lycopersicum esculentum* (tomato), *Vicia faba* (broad beans), *Trichosanthes anguina* (padwal), *Luffa cylindrica* (dhundal, sponge gourd), *Moringa oleifera* (drumstick), *Allium sativum* (garlic), *Zingiber officinale* (ginger) and *Daucus carota* (carrot).

Fruits.—*Prunus amygdalus* (almond), *Musa paradisiaca* (banana), *Carrisa carandas* (caranda), *Anacardium occidentale* (cashew nut), *Cocos nucifera* (coconut), *Psidium guajava* (guava), *Mangifera indica* (mango), *Carica papaya* (papaya), *Pyrus communis* (pear), *Pistacia vera* (pista), *Cydonia oblonga* (quince), *Tamarindus indica* (commercial tamarind) and *Juglans regia* (walnut).

(Miss) K. Ganju and (Miss) B. Puri.

565

TABLE I.
Rf values of authentic samples of flavonoids.

Substance.	Rf value.
Kampferol. ...	0.37
Quercetin ...	0.40
Quercitrin ...	0.90
Rutin ...	0.78
Morin ...	0.62
Robinetin ...	0.34
Myricetin ...	0.26
Quercetagetin ...	0.33
Gossypetin ...	0.62
Gossypin ...	0.86
Apigenin ...	0.52
Apin ...	0.70
Luteolin ...	0.54
Liquiritigenin ...	0.76
Iso-liquiritigenin ...	0.50
Liquiritin ...	0.87
Isoliquiritin ...	0.71
Naringenin ...	0.63
Naringin ...	0.87
Hesperetin ...	0.60
Hesperidin ...	0.84
Eriodictyol ...	0.80

Table II contains the materials which indicated the presence of bioflavonoids, but the quantity present was so small that their isolation, identification and estimation has not been possible. The results are tabulated in the form of Rf values and the suggested flavonoids (Table II).

On the other hand, the following leafy vegetables have revealed the presence of quercetin glycoside (quercitrin) in appreciable amounts. It has been possible to isolate, identify and estimate it as the quercetin content of the materials. Vitamin K has also been identified, isolated and estimated (Table II).

DISCUSSION.

An attempt has been made to isolate, identify and estimate the bioflavonoids present in indigenous vegetables and fruits. Among the large number of substances studied, it has been possible to isolate quercetin from eight leafy vegetables. The ordinary method of direct hydrolysis of the extract, without previous purification, did not give satisfactory results, as the extracts of the vegetables and fruits contained considerable quantity of waxes and other impurities. Hence, preliminary purification using lead-salt method was found necessary. It has been observed that in the materials which contain a good amount of flavonoid, appreciable quantity of vitamin K is invariably present.

The important physiological and biochemical rôle of bioflavonoids is their relationship with ascorbic acid. Bioflavonoids protect ascorbic acid against oxidation and ascorbic acid exercises a similar protective effect on the bioflavonoids. Supplementation of the diet of guinea-pigs with hesperidin and ascorbic acid was shown to produce a greater increase in growth rate than occurred when ascorbic acid was administered alone (Bhagwat, 1946). Bioflavonoids were shown to retard the

TABLE II.
Rf Values of extracts of vegetables and fruits before and after hydrolysis.

Name.	Rf values before hydrolysis.	Rf values after hydrolysis.	Suggested bioflavonoids.	Remarks.
VEGETABLES				
<i>Portulaca oleracea</i> (purslane kulfa)	0.87	0.78	Liquiritin	Used as vegetable and also as salad.
<i>Solanum melogena</i> (brinjals)	0.81	0.80	Eriodictyol	Unripe fruit used as vegetable.
<i>Coriandrum sativum</i> (coriander)	—	0.33, 0.51 0.73, 0.81	Quercetagenin, luteolin and eriodictyol	Fruits and leaves used as condiment.
<i>Lactuca sativa</i> (lettuce)	—	0.31, 0.82	Quercetagenin and eriodictyol	Used as salad.
<i>Allium cepa</i> (onions, bulb and leaves)	0.27, 0.42	0.28, 0.41	Quercetin and myricetin	Fresh leaves used as vegetable, bulbs more popular.
<i>Ipomoea batatas</i> (sweet potato)	0.28, 0.81	0.26, 0.80	Myricetin and eriodictyol	The vines used as green vegetables and the tuber is popular.
<i>Pisum sativum</i> (peas)	0.88	0.40	Quercitrin	Green peas used as vegetables, dried ones as pulses.
<i>Brassica oleracea</i> var. <i>capitata</i> (cabbage)	—	0.61	Unidentified	Used as green vegetable.
<i>Brassica oleracea</i> var. <i>botrytis</i> (cauliflower)	—	0.80	Unidentified	Used as green vegetable.
<i>Citrullus vulgaris</i> var. <i>fistulosus</i> (round gourd)	—	0.51	Luteolin	Used as green vegetable.
<i>Momordica charantia</i> (bitter gourd)	—	0.52, 0.87	Luteolin and one unidentified substance	Its green fruits are either fried or cooked.
<i>Cucumis sativus</i> (cucumber)	—	0.51	Luteolin	Eaten fresh and also cooked.
FRUITS				
<i>Emblica officinalis</i> (emblic)	—	0.40, 0.77	Quercetin and one unidentified substance.	It is a rich source of vitamin C. Fresh fruit studied.
<i>Malus sylvestris</i> (apple)	—	0.40	Quercetin	Dessert apple, fresh fruits studied.
<i>Prunus armeniaca</i> (apricot)	—	0.35	Kämpferol	Fresh fruits studied.
<i>Zizyphus mauritiana</i> (wood apple, ber)	—	0.41	Quercetin	Fresh fruits studied.

(Miss) K. Ganju and (Miss) B. Puri.

567

(TABLE II—Concl.)

Name.	Rf Values before hydrolysis.	Rf Values after hydrolysis	Suggested bioflavonoids.	Remarks.
Cape gooseberry (raspberry belongs to genus Rubus)	—	0.36	Kæmpferol	Fresh fruits studied.
Prunus aium (sweet cherry)	—	0.82	Eriodictyol	Fresh fruits studied.
Achras-sapota (sapota)	—	0.40	Quercetin	Fresh fruits studied.
Phoenix dactylifera (date)	—	0.40	Quercetin	Commercial product studied.
Ficus carica (fig)	—	0.41	Quercetin	Commercial product studied.
Vitis vinifera (grapes)	—	0.41	Quercetin	Commercial product studied.
Artocarpus heterophyllus (jack fruit)	—	0.35, 0.82	Kæmpferol and eriodictyol	Unripe used as vegetable.
Litchi chinensis (litchi)	—	0.81	Eriodictyol	Fresh fruit studied.
Morus alba (mulberry)	—	0.81	Eriodictyol	Fresh fruit studied.
Cucumis melo (musk melon)	—	0.82	Eriodictyol	Fresh fruit studied.
Prunus persica (peach)	—	0.35, 0.75	Kæmpferol and one unidentified substance	Fresh fruit studied.
Grewia asiatica (falsa)	—	0.41	Quercetin	Fresh fruit studied.
Ananas comosus (pine apple)	—	0.82	Eriodictyol	Fresh fruit studied.
Punica granatum (pomegranate)	—	0.55	Luteolin	Edible portion studied.
Prunus domestica (plum)	—	0.42	Quercetin	Fresh fruit studied.
Fragaria vesca (strawberry)	—	0.25, 0.81	Myricetin and one unidentified substance	Fresh fruit studied.
Citrus sinensis (sweet orange)	—	0.50	Hesperidin complex not fully identified	Fresh fruit studied.
Citrus aurantiifolia (lime)	—	0.51	Hesperidin complex not fully identified	Fresh fruit studied.
A variety of green orange (mosambi)	—	0.50	Hesperidin complex not fully identified	Fresh fruit studied.
Citrullus vulgaris (water melon)	—	0.54, 0.81	Luteolin and eriodictyol	Fresh fruit studied.

TABLE III.
Leafy vegetables showing vitamin P and vitamin K in parts
per million of the materials.

Name.	Rf values before hydrolysis.	Rf values after hydrolysis.	Bioflavo- noids (quercetin), parts per million.	Vitamin K, parts per million.	Remarks.
1. <i>Bassella alba</i> (Indian spinach 'poi')	0.89	0.40	505	200	Leaves are commonly used as vegetable.
2. <i>Trigonella foenum græcum</i> (Fenugreek, methi).	0.90	0.42	490	240	The leaves and young pods are used as vegetable and seeds medicinally and as a condiment.
3. <i>Mentha longi- folia</i> (mint)	0.88	0.40	502	200	The leaves are used in medi- cine and also for improving taste of food.
4. <i>Chenopodi- um album</i> (pig weed, bathua)	0.89	0.40	504	250	The leaves are used as vege- table.
5. <i>Amaranthus blitum oler- acea</i> (chulai, amarnathus)	0.88	0.40	500	220	Young leaves are used as vegetable.
6. <i>Brassica compestris</i> var. <i>sarson</i> (field mus- tard, sarson)	0.90	0.41	495	230	Leaves and tender stems are used as vegetable.
7. <i>Anethum graveolens</i> (soya)	0.89	0.42	500	240	The tender leaves and stems are used as vegetable.
8. <i>Spinacia oleracea</i> (spinach)	0.90	0.41	500	250	It is mainly used as vegetable.

appearance of symptoms of scurvy in guinea-pigs on a scorbutogenic diet (Lecoq-Chauchard, and Mazou'e, 1946). The basic mechanism involved in the relationship of bioflavonoids and ascorbic acid in the maintenance of capillary integrity was elucidated by Beiler and Martin (1947) who demonstrated *in vitro* that amounts of bioflavonoids which alone showed no effect on hyaluronidase, potentiated the inhibitory activity of ascorbic acid as much as two hundred to three hundred per cent. Evidence has also been provided linking the action of bioflavonoids to histamine. Hesperidin was shown to reduce the toxicity of histamine in normal animals. The enhanced histamine toxicity in guinea-pigs on scorbutogenic diets was prevented by catechin epimers (Parrot and Richet, 1945). Anaphylactic shock was also found to be prevented by soluble hesperidin compounds (Hiramatsu, 1941). Ungar (1945) believed that hesperidin methyl chalcone and epimerized D-catechin inhibited the release of histamine from blood cells. Martin *et al.* (1949) found that

flavono-
and pos-
mation

In
on hist-
epineph-
suggest-
on capil-
the rela-
antihæm-
prothro-
and seri-
results i-
of vitam-

T
capillari-
enormo-
this wa-
efficien-
impaired
of hespi-
rheuma-
Howeve-
animal

1.
filter-pa-
reaction

2.
vegetab

3.
presenc

T
for his

Ben-
Bia-
Cin-
Dai-
Far-
Fur-
Gu-

(Miss) K. Ganju and (Miss) B. Puri.

569

flavonoid compounds were effective inhibitors of histidine decarboxylase *in vitro* and postulated that they exerted their anti-anaphylactic effect by preventing the formation of histamine.

In addition to potentiation of ascorbic acid, inhibition of hyaluronidase, effect on histamine and histidine decarboxylase as mentioned above, inhibition of epinephrine oxidation and decrease in bleeding and coagulation time have also been suggested as contributing mechanisms by which the flavonoids exert their influence on capillary fragility and permeability. Their effect on coagulation time indicates the relationship between bioflavonoids and vitamin K—the coagulation vitamin or antihæmorrhagic vitamin. Deficiency of vitamin K results in reduction of plasma prothrombin concentration; the coagulation time of the blood is thus prolonged and serious hæmorrhages may occur. According to Dam (1953) vitamin K deficiency results in the lack of more than one coagulation factor. How exactly the presence of vitamin K influences the activity of bioflavonoids has not been clearly elucidated.

The intercellular cement substance is essential to the normal integrity of the capillaries. It is obvious that any slight change in the nature of the cement will enormously affect the permeability of the capillary wall and hence diffusions across this wall of all life-sustaining elements. Numerous clinical reports show the efficiency of hesperidin and ascorbic acid in many disease states associated with impaired function of the capillary tree. Beneficial results from the administration of hesperidin and ascorbic acid have also been reported in such conditions as rheumatic fever, rheumatoid arthritis, diabetic retinopathy and vascular purpuras. However, much research must be done before the rôle of flavonoids in therapy, in animal nutrition or even in plant metabolism is understood.

SUMMARY AND CONCLUSIONS.

1. A systematic survey for the presence of bioflavonoids by the method of filter-paper chromatography (horizontal migration) and their characteristic colour reactions has revealed their presence in large number of vegetables and fruits.

2. Quercitrin (quercetin glycoside) has been isolated from the eight leafy vegetables in the form of its quercetin content (about 500 parts per million).

3. The vegetables from which quercetin was isolated also indicated the presence of vitamin K, i.e. about 200 to 250 parts per million.

Thanks are due to C.S.I.R. for financial assistance and to Prof. T.R. Seshadri for his valuable advice.

REFERENCES.

- BEILER, J.M., and MARTIN, G.J. (1947) ... *Jour. Biol. Chem.*, **171**, p. 507.
BHAGWAT, K. (1946) ... *Ind. Jour. Med. Res.*, **34**, p. 87.
CHATTERJEE, D., and RANDHAWA, G.S. (1952) *Indian Jour. Hort.* **9** (2) p. 24-36.
... *Ibid.* **9** (4) : p. 64-84.
DAM, H. (1953) ... *Proc. Nutr. Soc.*, **12**, p. 114.
FAROOQ M.O., GUPTA, S.R., KIAMUDDIN, M., ... *Jour. Sci. Industr. Res.*, **12 B**, p. 400.
... RAHMAN, W., and SESHADRI, T.R. (1953)
FUKUDA, T. (1932) ... *Arch. Exper. Path. Pharmacol.*, **164**, p. 685.
GUPTA, S.R., and SESHADRI, T.R. (1952) ... *Proc. Ind. Acad. Sci.*, **25 A**, p. 242.

- HIRAMATSU (1941) ... *Jap. Jour. Dermatol. Urol.*, 50, p. 37.
KOIKE, H. (1931) ... *Folia Pharmacol., Japan*, 12, p. 89.
LACQ, R., CHAUCHARD, P., and MAZOU'E, H. (1946) *Compt. Rend. Soc. Biol.*, 141, p. 52.
MARTIN, G.J., GRAFF, M., BRENDL, R., and BEILER, J.M. (1949) *Arch. Biochem.*, 21, p. 177.
PARROT, E.M., and RICHET, C. (1945) *Compt. Rend. Soc. Biol.*, 139, p. 1050.
PANKAJAMANI, K.S., and SESHADRI, T.R. (1952) *Proc. Ind. Acad. Sci.*, 36, p. 157-169.
RANGASWAMI, S., and SESHADRI, T.R. (1952) 'Chemistry of Vitamins and Hormones', pp. 69 and 76.
SESHADRI, T.R. (1948) *Jour. Ind. Chem. Soc., Ind. & News Ed.* 11, p. 35.
SZENT GYORGYI, A. (1936) *Curr. Sci.*, 5, p. 285.
Idem (1955-56) *Ann. N. Y. Acad. Sci.*, 61, Art. 3, p. 732-735.
UNGAR, H. (1945) *Endocrinology*, 37, p. 329.

Ind. J.

E

the hi
Longe
fatty a
the co
fat-fre
and li
acid.

feedin
choles

weigh
rats w
on die
groun
cent c
The r
1954).
0.5 g.
was n
were
13 we
analy
and c
blood
lent.
unsat

tissue
for fa

630 ESSENTIAL OILS OF THE PLANT FAMILY UMBELLIFERAE

apart, but the plants in each row are kept quite close. Dill, an annual crop, must be sown every year. The herb commences to grow at the end of May or the beginning of June. When the flowers turn yellow the plants are cut for use in pickles. If not cut, the flowers shortly thereafter turn to a deep yellow. In this state, too, the plants may be used for pickling purposes; in fact, this period (end of June) is the principal cutting season. During August the seeds develop and turn brown, the plants then becoming unsuitable for the flavoring of pickles. From the middle of August to mid-September the seeds mature fully and must be harvested very carefully. For this purpose the plants are cut with scythes or machines, then bundled and stacked up in the fields until all seeds become fully ripe and dry. Subsequently the material is transported into barns and threshed in machines. Finally the seed is winnowed.

SPANISH DILL HERB (WEED) OIL

Spain used to produce small quantities of dill herb oil, distilled from the overground parts of plants containing the green, unripe seed. These plants grow wild in the provinces of Huelva and Extremadura. The harvest takes place in June and July. Distillation of one charge lasts from 5 to 8 hr., 150 kg. of herb material yielding about 1 kg. of oil. Production of this type of oil could be stepped up to about 4,000 lb. per year, provided a sufficiently attractive price was paid for these oils. However, the odor and flavor of this type of oil is inferior to that of the Hungarian or American oils which are distilled from cultivated herb. The Spanish oils, distilled from wild growing plants, contain only a small percentage of carvone; they exhibit a strong phellandrene reaction.

CHEMICAL COMPOSITION OF DILL SEED OIL

Carvone. The main constituent, amounting to 40 to 60 per cent of the oil, was identified by Gladstone⁸ and by Beyer.⁹ It is identical with the carvone occurring in caraway seed oil.

d-Limonene. Found by Wallach¹⁰ as the principal terpene. It is present in the fraction b. 175°-180° and was identified as tetrabromide m. 104°-105°.

Phellandrene. The Schimmel chemists¹¹ obtained a positive reaction with sodium nitrite and glacial acetic acid in an English oil, also in Spanish oils, i.e., in those dill oils which are distilled from the seed and herb. German oils, distilled exclusively from seed, gave a positive phellandrene reaction only if the first fraction was tested.

⁸ *J. Chem. Soc. (London)* 25 (1872), 1-25. *Jahresber. Chem.* (1872), 816.

⁹ *Arch. Pharm.* 221 (1883), 283.

¹⁰ *Liebigs Ann.* 227 (1885), 292.

¹¹ *Ber. Schimmel & Co.*, April (1897), 16; October (1898), 20.

Paraffins. C
leum eth

Dillapiol
has not be

The abov
oils of Eur
oil contains

α -Pinene. T

Dipentene.

Dihydrocarv
fraction

Accordin
and dihydr

The Schi
tilled from

d- α -Phelland
113°.

Terpinene.
terpinen

Limonene or

Carvone. F

Dillapiole.
151°.

Isomyrsticin
proved t
by mixe
Oxid
tinal

Myristicin.
tion by
ration

In th
tified, v

¹² *Ibid.*, Apr

¹³ *Am. P*

¹⁴ Private

¹⁵ *Ber. Sch*

¹⁶ *Ibid.*

te close. Dill, an annual crop, begins to grow at the end of June. When the flowers turn yellow the plants are ready for harvest. The flowers shortly thereafter turn white. The plants may be used for pickling. The principal cutting season is in the fall. When the plants are grown, the plants then become ready for harvest. From the middle of August to the middle of September must be harvested very carefully with scythes or machines, then the seeds become fully ripe and are threshed in

SEED) OIL

Dill herb oil, distilled from the green, unripe seed. These plants are ready for harvest. The harvest takes place in the fall. The charge lasts from 5 to 8 hr., and the yield is 100 lb. of oil. Production of this oil is 1000 lb. per year, provided a good yield. However, the odor and taste of the Hungarian or American oils are different. The Spanish oils, distilled from the seed, contain all percentage of carvone; they

DILL SEED OIL

to 60 per cent of the oil, was identical with the carvone occurring

terpene. It is present in the fraction m. 104°-105°.

a positive reaction with sodium is also in Spanish oils, i.e., in those of the herb. German oils, distilled exclusively from the seed, give a reaction only if the first fraction

OIL OF DILL

631

Paraffins. Occur in the fractions boiling above carvone. Crystallized from petroleum ether, they melt at 64°.

Dillapiole b. 285°, which occurs in Indian seed oil (*Anethum sowa* D.C.), has not been found in European oils distilled exclusively from seed.¹²

The above mentioned constituents were identified years ago in dill seed oils of European origin. More recently, Branigan¹³ reported that dill seed oil contains also

α -Pinene. Traces only; nitrobenzylamine m. 123.1°.

Dipentene. Tetrabromide m. 125°.

Dihydrocarvone. Identified as dibromide m. 70.4° and as oxime m. 89° in a small fraction of dill oil produced from American seed.

According to the same worker,¹⁴ small quantities of α -pinene, dipentene, and dihydrocarvone occur in both European and American dill seed oils.

CHEMICAL COMPOSITION OF DILL HERB OIL

The Schimmel chemists¹⁵ identified the following compounds in oil distilled from dill herb:

d- α -Phellandrene. The main constituent, $\alpha_D + 88^\circ 22'$, $d_{15} 0.8494$. Nitrite m. 109°-113°.

Terpinene. Identified as nitrite m. 155°-156°, dihydrochloride m. 51°-52°, and as terpinene terpin m. 136°-137°.

Limonene or Dipentene. *Cis*-terpin hydrate m. 116°-117°.

Carvone. Present in much smaller quantities than in the seed oil.

Dillapiole. Conversion into dillisoapiole m. 44°-45°, also dillapiolic acid m. 150°-151°.

Isomyristicin. Originally mistaken for dillisoapiole, this compound m. 44° finally proved to be isomyristicin $C_{11}H_{12}O_3$ which also occurs in mace oil; confirmation by mixed melting point.

Oxidation with ozone and reductive splitting of the ozonide easily gave myristinaldehyde m. 131°.

Myristicin. The same investigators¹⁶ identified myristicin $C_{11}H_{12}O_3$ in the fraction b₄ 126°, $d_{20} 1.1442$, $n_D^{20} 1.5407$; confirmed by combustion analysis and preparation of dibromomyristicin dibromide m. 130°.

In the high boiling fractions a bluish compound and waxes, both not yet identified, were noticed.

¹² *Ibid.*, April (1897), 16.

¹³ *Am. Perfumer* 48 (Feb. 1946), 69.

¹⁴ Private communication by Mr. G. V. Branigan, New York.

¹⁵ *Ber. Schimmel & Co.*, April (1903), 24; October (1908), 38; (1927), 25.

¹⁶ *Ibid.*

632 ESSENTIAL OILS OF THE PLANT FAMILY UMBELLIFERAE

In a more recent publication, Branigan¹⁷ lists α -pinene and camphene as constituents of dill herb oil, but does not indicate how he identified these terpenes.

Steam distilling a concentrated extract of dried dill herb, Elze¹⁸ obtained a volatile oil, d_{15} 0.903, $\alpha_D +68^\circ$, which contained *n*-octyl alcohol b. 190° – 192.5° , d_{15} 0.830.

USE OF DILL HERB OIL

The employment of dill herb oil produced from the whole overground part of the plant has become increasingly extensive in the United States and Canada. At first, it was used primarily to flavor processed dills produced from salt stock, and in many cases it completely replaced the dill herb itself for that application. The lack of uniformity of flavor, obtained from the use of dill herb in so-called genuine dills, later prompted many manufacturers to supplant the herb with the corresponding oil, to accentuate and standardize the flavor. This now constitutes a very regular practice, with an increasing tendency to depend more and more on the oil and less on the herb itself.

Fabian,¹⁹ in the course of investigations on the conservation of spices in food manufacture, found that dill herb actually absorbs some of the essential oils from some of the other spices (pimenta, cassia, bay leaves, mustard, celery seed, chili, peppers, cardamom, and ginger root) employed for making dill pickles. The same author demonstrated the great waste of essential oils when whole spices are used.

Since oil of dill herb is not particularly soluble in the acid brine used for dill pickles, it is very important for its successful employment that due steps be taken to insure as complete a solution as possible.

This involves first cutting or dissolving the oil with some neutral solvent, followed by the addition of this oil solution to the brine during vigorous and fairly prolonged agitation of the latter. Such agitation is frequently accomplished by means of a high-speed pump, e.g., a centrifugal pump, which repeatedly circulates the brine in and out of the mixing tank. Another device consists of a high-speed electric mixer, the shaft of which is long enough so that the propellers come close to the bottom of the tank, insuring a complete circulation of the contents.

Only after the oil is completely dispersed in the brine should the latter be used to cover the pickles.

For diluting the oil, alcohol is occasionally employed, but it can be replaced by glacial acetic acid. In other cases, the oil is reduced to 5 or 10 per cent strength in the form of an emulsion, with gum acacia or any other

¹⁷ *Am. Perfumer* 48 (February 1946), 65. ¹⁹ *Food in Canada*, October (1942).

¹⁸ *Riechstoff Ind.* (1926), 192.

suitable
in some s

It has
more rapid
words, if
in it for
which de
hand, thi
become s
condition
treatment
individual

This a
oil of dil
plies the
20 gal. o

Oil of
tions des
diments.

Use of
agent by
popular
has decli
high carv
as a sub

For a
cultivate
or wheth
plant ha
the oils
their phy
Sowa pla

The yi
1.20 to 3

Physic
the prop
following

20 "Die At

DILL SEED OIL, EUROPEAN

DESCRIPTION

The volatile oil obtained by steam distillation from the crushed dried fruit (or seeds) of *Anethum graveolens*, L. (Fam. *Umbelliferae*), grown in various European countries. It is a slightly yellowish to light yellow liquid with a caraway-like odor and flavor. It is soluble in most fixed oils and in mineral oil. It is soluble, with slight opalescence, in propylene glycol, but it is practically insoluble in glycerin.

SPECIFICATIONS

Assay. Not less than 42 per cent and not more than 60 per cent, by volume, of ketones as carvone ($C_{10}H_{14}O$).

Angular rotation. Between $+70^\circ$ and $+82^\circ$.

Refractive index. Between 1.4830 and 1.4900 at 20° .

Solubility in alcohol. Passes test.

Specific gravity. Between 0.890 and 0.915.

Limits of Impurities

Arsenic (as As). Not more than 3 parts per million (0.0003 per cent).

Heavy metals (as Pb). Not more than 40 parts per million (0.004 per cent).

Lead. Not more than 10 parts per million (0.001 per cent).

TESTS

Assay. Proceed as directed under *Aldehydes and Ketones—Neutral Sulfite Method*, page 742.

Angular rotation. Determine in a 100-mm. tube as directed under *Optical Rotation*, page 780.

Refractive index, page 785. Determine with an Abbé or other refractometer of equal or greater accuracy.

Solubility in alcohol. Proceed as directed in the general method, page 746. One ml. dissolves in 2 ml. of 80 per cent alcohol, with slight opalescence which may not disappear on dilution to as much as 10 ml.

Specific gravity. Determine by any reliable method (see page 4).

Arsenic. A *Sample Solution* prepared as directed for organic compounds meets the requirements of the *Arsenic Test*, page 720.

Heavy metals. Prepare and test a 500-mg. sample as directed in *Method II* under the *Heavy Metals Test*, page 763, using 20 mcg. of lead ion (Pb) in the control (*Solution A*).

Lead. A *Sample Solution* prepared as directed for organic compounds meets the requirements of the *Lead Limit Test*, page 772, using 10 mcg. of lead ion (Pb) in the control.